

Volume 7

Pages 1377 - 1634

UNITED STATES DISTRICT COURT

NORTHERN DISTRICT OF CALIFORNIA

Before The Honorable Susan Illston, Judge

VERINATA HEALTH, INC., et al.,)

Plaintiffs,)

VS.)

NO. C 12-05501 SI

ARIOSIA DIAGNOSTICS, INC., et)

al.,)

Defendants.)

San Francisco, California
Thursday, January 18, 2018

TRANSCRIPT OF PROCEEDINGS

APPEARANCES:

For Plaintiffs Verinata Health, Inc.; Illumina, Inc.:
Weil, Gotshal & Manges LLP
201 Redwood Shores Parkway
Redwood Shores, California 94065
(650) 802-3000
(650) 802-3100 (fax)

**BY: CHRISTOPHER J. COX
HANNAH L. JONES
CHRISTOPHER S. LAVIN
EDWARD ROBERT REINES
DEREK C. WALTER**

Reported by Lydia Zinn, CSR 9223, RPR, FCRR, Official Reporter

APPEARANCES:

For Defendant Ariosa Diagnostics, Inc.:
Irell & Manella LLP
1800 Avenue of the Stars
Suite 900
Los Angeles, CA 90067
(310) 277-1010

**BY: CASEY MAE CURRAN
DAVID ISAAC GINDLER
ALAN J. HEINRICH
MOLLY JEAN RUSSELL
SARA ADINA STOHL**

For Defendant Ariosa Diagnostics, Inc.:
Irell & Manella LLP
840 Newport Center Drive, Suite 400
Newport Beach, California 92660-6324
(949) 760-0991
(949) 760-5200 (fax)

**BY: LISA SHARROCK GLASSER
SANDRA LINETTE HABERNY**

Also Present: Jeffrey Eidel

I N D E X

Thursday, January 18, 2018 - Volume 7

DEFENDANT'S WITNESSESPAGE VOL.QUACKENBUSH, JOHN

(SWORN)	1382	7
Direct Examination resumed by Mr. Heinrich	1383	7
Cross-Examination by Mr. Reines	1421	7
Redirect Examination by Mr. Heinrich	1451	7
Recross-Examination by Mr. Reines	1457	7

CANTOR, CHARLES

(SWORN)	1458	7
Direct Examination by Ms. Haberny	1459	7
Cross-Examination by Mr. Reines	1481	7
Redirect Examination by Ms. Haberny	1505	7
Recross-Examination by Mr. Reines	1511	7

HARRIS, CRANE

By Videotape Deposition (not reported)	1515	7
--	------	---

YEE, JEAN

(SWORN)	1517	7
Direct Examination by Ms. Curran	1517	7
Cross-Examination by Mr. Reines	1525	7
Redirect Examination by Ms. Curran	1529	7

SULLIVAN, RYAN MICHAEL

(SWORN)	1531	7
Direct Examination by Ms. Glasser	1531	7
Cross-Examination by Mr. Cox	1567	7

PLAINTIFFS' WITNESSESPAGE VOL.COOPER, GREGORY MICHAEL

(SWORN)	1589	7
Direct Examination by Mr. Walter	1590	7
Cross-Examination by Mr. Heinrich	1621	7

1	<u>E X H I B I T S</u>			
2	<u>TRIAL EXHIBITS</u>	<u>IDEN</u>	<u>EVID</u>	<u>VOL.</u>
3	507A		1618	7
4	718	1514		7
5	1044		1464	7
6	1059		1566	7
7	1087		1566	7
8	1102		1566	7
9	1133		1566	7
10	1160		1566	7
11	1226		1566	7
12	1252		1566	7
13	1318		1566	7
14	1362		1566	7
15	1385		1566	7
16	1396-11		1566	7
17	1396-12		1566	7
18	1396-40		1566	7
19	1396-41		1566	7
20	1414		1566	7
21	1587		1566	7
22	1589		1566	7
23	1590		1566	7
24	1591		1566	7
25	1594		1566	7

I N D E XE X H I B I T STRIAL EXHIBITSIDEN EVID VOL.

1608	1566	7
1615	1566	7
1648	1566	7
1649	1566	7
1650	1566	7
1651	1566	7
1660	1516	7
1661	1516	7
1662	1516	7
1663	1516	7
1664	1516	7

1 Thursday - January 18, 2018

8:40 a.m.

2 P R O C E E D I N G S

3 ---000---

4 (Proceedings were heard outside the presence of the jury:)

5 **THE COURT:** There were issues about the instructions;
6 you want to talk about that now or later?

7 **MR. REINES:** Oh, I don't think so. I think we were
8 just -- we wanted to confer among the lawyers further.

9 **THE COURT:** Okay.

10 **THE CLERK:** Oh, about the form, though, of being
11 submitted.

12 **THE COURT:** We can talk about that later. Just
13 remind me.

14 **MR. GINDLER:** Yeah, of course. Thank you.

15 (Proceedings were heard in the presence of the jury:)

16 **THE COURT:** You're still under oath, sir, from
17 before.

18 **THE WITNESS:** Right.

19 **THE COURT:** Oh, go ahead and swear the witness.

20 **THE CLERK:** Might as well just to be sure.

21 JOHN QUACKENBUSH,

22 called as a witness for the Defendants, having been duly sworn,
23 testified as follows:

24 **THE WITNESS:** I do.

25 **THE CLERK:** Thank you.

1 **THE COURT:** I wanted to tell you one thing, ladies
2 and gentlemen, before we get going.

3 Today is Thursday, so it's our last day together this
4 week, and we'll meet again on Monday.

5 Between now and then, the United States Government may or
6 may not shut down. I don't know. But we have enough money to
7 run the judiciary next week. So you have to come back Monday
8 even if there's a government shutdown. I just wanted to let
9 you know that.

10 All right. You may proceed.

11 **DIRECT EXAMINATION (resumed)**

12 **BY MR. HEINRICH**

13 **Q.** Good morning, ladies and gentlemen.

14 Welcome back, Professor Quackenbush.

15 **A.** Good morning.

16 **Q.** So we've had a lot of scientific terms whizzing around for
17 the past week and a half.

18 Why don't we take a few minutes and just talk about what
19 these terms mean.

20 **A.** Okay.

21 **Q.** So we've been talking about DNA. Where is DNA normally
22 found?

23 **A.** So DNA is fund in our cells. Remember yesterday I was
24 talking about the Genome Project and the cell being like a
25 machine to make protein -- made of proteins.

1 The blueprint for those proteins is recorded in the genes,
2 in the DNA. The DNA is packaged in bodies called
3 "chromosomes," and the chromosomes, themselves, are in the
4 nucleus of the cell.

5 So DNA is in the chromosomes inside the cell.

6 **Q.** And what's the typical structure of DNA?

7 **A.** So DNA is an abbreviation. It's deoxyribonucleic acid.

8 DNA is a double-stranded molecule, so there are two
9 strands. The yellow band is deoxyribose -- that's the sugar --
10 and these little bars in between them, it sort of winds up like
11 a spiral staircase, those are the bases of nucleic acids.

12 **Q.** So how do the bases interact with each other?

13 **A.** So if you look at the slides, the four bases -- adenine,
14 cytosine, guanine and thymine -- are A, C, G, T. And the
15 reason DNA can store a code is because the As and Ts across the
16 strands pair, and the Gs and Cs across the strands pair, and we
17 have a positive and a negative - two strands joined together.

18 **Q.** And is this referred to as "complementary bases"?

19 **A.** So the bases are complementary to each other, yes.

20 **Q.** And is that concept of complementary bases related to the
21 term "hybridization" that we've been talking about?

22 **A.** Sure. There are a couple of things we talk about in the
23 context of these inventions and Ariosa's products, and it's the
24 idea of denaturation; right?

25 So DNA is double-stranded, but the strands can separate.

1 That's how DNA can be copied. We can do that in the lab by
2 just feeding the DNA, and the strands come apart -
3 denaturation. And then we if we pull them back down at the
4 appropriate temperature, they can come back together with the
5 complementary bases pairing to each other.

6 Q. And that's called "hybridization"?

7 A. That's hybridization, sometimes referred to -- also as
8 "annealing."

9 Q. Okay. What's cell-free DNA?

10 A. So over the course of your lifetime, your cells grow,
11 divide, and sometimes they die. And when they die, they
12 actually break open. In the process of dying, a lot of enzymes
13 are released in the cell, and it breaks the DNA up into
14 fragments. So these fragments are released from the cell, and
15 they can be absorbed, you know, into other fluids in your body,
16 like your bloodstream.

17 Q. And then what's fetal cell-free DNA?

18 A. Sure. So the fetus is developing in -- in the uterus, and
19 inside the placenta. And even though we think about the fetus
20 growing and, you know, developing, some of its cells are dying,
21 too. So they're releasing DNA into the amniotic fluid around
22 the fetus. That DNA then moves through the placenta into the
23 mother's bloodstream.

24 And the little cartoon at the right is showing that white
25 DNA, that's fetal DNA, but it's in the background of all of the

1 maternal DNA; right? The mother is much bigger than the fetus,
2 so she's going to be shedding a lot more DNA. But in her
3 bloodstream, we have a mix of her DNA and DNA from her fetus.

4 **Q.** So let's get into your non-infringement opinion with
5 respect to the '794 patent.

6 **A.** Sure.

7 **Q.** So what do Steps A and B of Claim 1 of the '794 patent
8 require?

9 **A.** So Step A requires that we have a single-stranded target
10 sequence. So it's a sequence we ultimately want to detect.
11 It's got to be single-stranded, and it's attached to a first
12 solid support. So in this case it's a bead to which a
13 single-stranded DNA molecule is attached.

14 And then if we look at Step B, it says contacting those
15 single-stranded target sequences with probes that can hybridize
16 to them to form hybridization complexes.

17 So it's a two-step process, A and then B.

18 **Q.** So how does that differ from what Ariosa does in
19 Harmony™?

20 **A.** Well, the '794, as I just mentioned, first attaches
21 single-stranded DNA, then forms these hybridization complexes.

22 What the Harmony™ assay does in Ariosa -- for Ariosa is,
23 first, does a hybridization; and then once we have
24 hybridization complexes, so the DNA is no longer single
25 stranded, it's attached to beads.

1 Q. Are there differences between those two approaches to
2 hybridization?

3 A. Sure. There are lots of differences.

4 Dr. Oliphant talked about some of the problems two days
5 ago on doing solid phase hybridization. Liquid phase
6 hybridization, which is allowing the probes and the targets to
7 interact in solution, is actually much, much more efficient.
8 It gives you a better result, because you have molecules moving
9 around, and they can more easily find each other.

10 Q. And what has the Court said about the order of steps A and
11 B?

12 A. So the Court has instructed us that when we look and
13 consider infringement, that Step A has to be performed before
14 Step B. So the order actually matters.

15 Q. All right. So let's start with the Harmony™ Version 2
16 assay.

17 What is this figure from?

18 A. So this is a figure from one of the Harmony™ SOPs.

19 Q. All right. And this is Trial Exhibit 67.

20 And what does this figure show?

21 A. So this is Figure 1 from the SOP. The SOP is basically a
22 set of descriptions, Standard Operating Procedure, that
23 instructs people in the lab how to carry the -- carry out the
24 assay. And this is showing the general order of steps in the
25 assay.

1 Q. And what do we see there, the first orange stick figure on
2 the right?

3 A. So on the right-hand side you see DNA being denatured.
4 This molecule called "biotin" is attached, and then it's
5 contacted by these probes, and the probes form these
6 hybridization complexes.

7 Q. And what's the structure of the DANSR probe that Ariosa
8 has come up with?

9 A. So because they want to be very specific, they have to use
10 a complex set of probes.

11 There are three probes for every target. So the little
12 green one in the middle, that's a probe that's designed just to
13 find the target sequence.

14 If you look at the probes in the left-hand side and
15 right-hand side, those are probes which also bind to the target
16 sequence. And once you get one, two, three together, perform
17 another operation called "ligation," those pieces on the end
18 become important.

19 So those pieces on the end are used in later steps for
20 amplification, making many copies of these, and detection.

21 Q. And does a target have to be -- has to hybridize to all
22 three probes in order to be detected, ultimately?

23 A. Right. If you only had one or two, you'd never be
24 detected, because you couldn't carry on the other steps in the
25 process.

1 Q. All right. So let's turn to the first step of the
2 hybridization process in Version 2 of Harmony™.

3 Can you explain this?

4 A. Sure. So this is just a little cutout from that cartoon
5 you saw earlier. And this is just showing the three probes
6 hybridized, or annealed, to an example target DNA molecule.

7 Q. Does the standard operating procedure, Exhibit 67, explain
8 what happens during this step?

9 A. Right. I mean, it -- it literally calls out the fact that
10 we have -- or not "we," but Ariosa has annealed these DANSR
11 oligonucleotides to the target DNA.

12 Q. And this is sections 13.4 and 13.5?

13 A. Yes.

14 Q. How long are these DANSR probes in the solution with the
15 target sequences?

16 A. So it's at least two hours; right?

17 We heard from Dr. Oliphant the other day that these are
18 added by a robot in the lab at room temperature. It's then put
19 in a device called a "thermocycler." So this is used to
20 precisely control temperature. And it sits in that
21 thermocycler for two hours.

22 Q. All right. So you were here in court when Dr. Cooper
23 testified?

24 A. Yes, I was.

25 Q. Did Dr. Cooper make some mistakes in describing the

1 conditions of this hybridization reaction?

2 **A.** Yes, a number of them.

3 **Q.** Was he mistaken about the starting temperature for the
4 reaction?

5 **A.** Yes. He said the starting temperature was 70 degrees. As
6 Dr. Oliphant told us, it's room temperature, which is about
7 20 degrees Celsius.

8 **Q.** And how do you know that?

9 **A.** Well, in addition to the fact that Dr. Oliphant told us
10 that, one of the words that was up there in that protocol was
11 TECAN. And TECAN is a robot that pipettes; it transfers
12 liquid, and it does that in the room at room temperature. So
13 it starts there.

14 The rest of the protocol actually defines how the
15 temperature changes in the thermocycler from -- from 70 degrees
16 down to, I think, 30 degrees.

17 **Q.** Dr. Cooper was also suggesting that probes and targets
18 wouldn't stick or hybridize at 70 degrees. We're talking about
19 Celsius?

20 **A.** 70 degrees Celsius, yes.

21 **Q.** Is that correct?

22 **A.** That's not correct.

23 In fact, there are other places in the protocol that talk
24 about another technique called "PCR," and the hybridization
25 there is carried out at 72 degrees C.

1 Q. What temperature does Ariosa use when it wants the strands
2 to come apart, or denature?

3 A. It heats the solution up to 95 degrees.

4 Q. And did Dr. Cooper have some mistaken assumptions about
5 the concentration of probes to targets?

6 A. Yes. Dr. Cooper said there were a few thousand.

7 As Dr. Oliphant pointed out, there are millions, in fact,
8 tens of millions. For every target sequence, you have tens of
9 millions, not only one, but all three probes; right?

10 So he said between 10 and 50 of each probe. So for every
11 molecule, you've got between 30 and 150 million probes floating
12 around; right.

13 Q. And were those mistakes by Dr. Cooper significant?

14 A. They're substantial mistakes, yes.

15 Q. And why is that?

16 A. Well, you know, if you think about the conditions, at
17 20 degrees Celsius, so room temperature -- right? -- our DNA is
18 stable, it's not flying apart. And these molecules -- you have
19 a target molecule surrounded by 150 million things looking for
20 it. They're going to bind. They're going to stick. They're
21 going to form hybridization complexes. Those are going to
22 survive at 70 degrees C; and then as temperatures cool back
23 down, they're more and more going to bind. And if you get more
24 things stacked together, the binding becomes even stronger.

25 Q. All right. So what's the next step after the probes and

1 target sequences hybridize?

2 **A.** Right. So the next step involves adding the beads. And
3 the reason you add the beads is you want to pull these
4 complexes out of solution. So they're added. And the biotin
5 molecule that then attached earlier binds to the compound of
6 the outside of the bead called "streptavidin."

7 **Q.** And what does the SOP explain about this step?

8 **A.** Well, you know, it tells us that now this annealed DNA --
9 right? -- the double-stranded complexes are attached to the
10 beads.

11 **Q.** And that's 13.6 of Trial Exhibit 67?

12 **A.** Yes.

13 **Q.** Okay. So let's summarize, in light of the claim
14 requirements.

15 Is Step A met in the DANSR Version 2 assay?

16 **A.** No. There -- we don't have single-stranded target DNA
17 attached to a solid support, when you look at -- at the Ariosa
18 Harmony™ Version 2 assay.

19 **Q.** And is Step B met?

20 **A.** No. Step B requires taking single-stranded DNA attached
21 to a bead and adding probes. The probes are added when the
22 DNA's still floating around, and only then are double-stranded
23 pieces attached to the beads.

24 **Q.** Well, what does Dr. Cooper base his infringement theory on
25 then?

1 A. Well, Dr. Cooper makes a guess.

2 Q. And what's that guess?

3 A. He guesses that there's some single-stranded targets that
4 somehow float around in -- for two hours under conditions that
5 are designed to drive hybridization with 50 to 150 million
6 probes floating around them, and that somehow they miss
7 hybridization, and then after they're bound to the beads
8 suddenly find partners.

9 Q. So is there any support for his -- his guess?

10 A. No, none whatsoever.

11 Q. So let's assume that Dr. Cooper is right, that some small,
12 tiny fraction of single-stranded sequences don't hybridize in
13 that two-hour hybridization step.

14 Would that, alone, be enough for plaintiffs to meet their
15 burden to prove infringement?

16 A. No, it wouldn't.

17 Q. And let's take a look at what Dr. Cooper is saying would
18 happen, aside from this failure to hybridize.

19 So what is this?

20 A. So this is a screen grab from the animation that he
21 showed.

22 Q. What do we see here, and what is he trying to show?

23 A. So if you look at this, you see, you know, a few of these
24 probes, not millions, surrounding the target sequences. And
25 there's one down here in the lower left that has bound one

1 oligo. There's another one over here sort of in the upper
2 right that hadn't found any partners yet.

3 Q. And then what does Dr. Cooper say happens?

4 A. So after these two hours, the beads are added; and so the
5 beads will bind to these biotins. And this lonely guy is still
6 over here by himself single-stranded.

7 Q. And then what does Dr. Cooper show?

8 A. If you look at the animation, then suddenly after not
9 finding partners for three hours, he finds all three.

10 Q. Now, what evidence does Dr. Cooper present to explain why
11 this lonely target sequence here couldn't find even a single
12 probe for that two-hour hybridization step, and then after
13 attachment suddenly finds all three probes?

14 A. None. And we know it's much more difficult when you're
15 bound to a solid to even find a probe, because you're not
16 moving around, and there's all this other stuff around you.

17 Q. All right. Let's turn to Version 1 of the Harmony™ assay.

18 A. Okay.

19 Q. Does Dr. Cooper say there's a big difference between
20 Version 1 and 2, or a small difference with respect to the
21 hybridization and attachment process?

22 A. Dr. Cooper actually says there's a very small difference
23 between them.

24 Q. And do you agree with that?

25 A. Yes, I do.

1 Q. And what is that small difference?

2 A. So the difference is that in Harmony™ Version 1, Ariosa
3 added the beads and the probes simultaneously on the robot.

4 Q. So, now, Dr. Cooper pointed to this figure (indicating).

5 A. Right.

6 Q. But is this somehow an indication that the beads are added
7 first before the probes?

8 A. No. This is the -- so this is a cartoon from the Standard
9 Operating Procedure for Harmony™ Version 1. And what it shows
10 is really a very short cartoon, but it illustrates the reason
11 why you add the biotin; right? You want to pull that DNA out
12 of the solution. And this is really designed to help the
13 people running the assay understand why they're carrying out
14 various steps in the process.

15 Q. Is there really any dispute about the fact that the beads
16 and the probes are added simultaneously in Version 1?

17 A. No, that's what the SOP says.

18 Q. Okay. So do the conditions of this reaction in Version 1
19 drive hybridization first or attachment first?

20 A. Again, this is happening at room temperature. We have 30
21 to 150 million copies of every single probe. There are
22 conditions in which the target sequences are going to find
23 their probes long before they bind.

24 Q. All right. And is your opinion supported by testimony
25 from one of the inventors of the '794 patent?

1 **A.** Yes. Dr. Fan, who's one of the inventors, in fact, says
2 that if you look at what happens, because of the kinetics of
3 solution hybridization, all of these molecules moving around
4 very quickly bumping into each other, that a hybridization is
5 much more likely to occur before the beads bind.

6 **Q.** Now, does Dr. Cooper make the same mistakes regarding his
7 assumptions on the reaction conditions for Version 1 as he does
8 for Version 2?

9 **A.** Yes, he makes mistakes about the concentration of the
10 oligos, the temperature, a number of other factors.

11 **Q.** Okay. Can you summarize your non-infringement opinions on
12 these elements?

13 **A.** Sure. It's pretty simple. Remember we have to do A and
14 then B; right? We'd have to do those two things in order if an
15 invention was going to occur, or a product was going to
16 infringe.

17 So first, single-stranded target sequences have to be
18 provided attached to a support, and then probes have to be
19 added; and that simply doesn't happen.

20 What the Ariosa Harmony™ assays do is first attach probes
21 to DNA, and then bind the hybridization complexes.

22 **Q.** So as a result, does either Version 1 or Version 2
23 infringe any claim of the '794 patent?

24 **A.** No, it doesn't.

25 **Q.** And, in fact, are elements A and B required for all of the

1 asserted claims?

2 **A.** Yes. You have to do A and B to practice Claim 1, and you
3 have to practice Claim 1 to practice any of the other claims.

4 **Q.** Now, could we just stop here for non-infringement
5 purposes?

6 **A.** No.

7 **Q.** Well --

8 **A.** Well, I guess we could, yeah, but there are some other
9 elements that are probably worth talking about.

10 **Q.** Okay. So what additional element are you going to address
11 for Version 2 of Harmony™?

12 **A.** So if we look at element 1F, element 1F talks about the
13 addition of amplicons, or -- about the binding of amplicons,
14 and their detection.

15 **Q.** Okay. And what's the second solid support that Illumina
16 is pointing to?

17 **A.** So here in Claim Element F, it says "immobilizing
18 amplicons to a second solid support;" and the second solid
19 support in Version 2 is a DNA microarray.

20 **Q.** All right. So does Harmony™ Version 2 actually immobilize
21 amplicons to that microarray?

22 **A.** No, it doesn't.

23 **Q.** All right. So let's talk about amplicons.

24 What guidance has the Court provided on the meaning of the
25 term "amplicon"?

1 A. Sure. So the Court has instructed us that when we see the
2 word "amplicon," this is something which is an amplification
3 product. So we run this procedure called "polymerase chain
4 reaction" -- PCR -- to make copies, and the copies are made
5 from modified probes.

6 So the amplicons are many, many copies of modified probes.

7 Q. And what guidance has the Court provided on what a
8 modified probe is?

9 A. All right. So the modified probe has to contain some
10 elements. It has to contain a universal priming site. And
11 remember I talked about those handles that were on the end of
12 the outside oligos? Those have priming sites, and then it also
13 has to have a piece which can hybridize -- right? -- come down
14 and bind to a target sequence.

15 Q. And are those modified probes then copied in the DANSR
16 Version 2 assay?

17 A. Yes, they're copied in the assay.

18 Q. And are they copied in whole, or is the entire modified
19 probe copied in DANSR Version 2?

20 A. So this is another piece of that figure from the SOP. And
21 what you can see in the upper part in the little red box are
22 those probes. Now, they've been joined together through a
23 process called "ligation." So the three landed, and they got
24 bound together.

25 And then those handles won't stick in a human genome, but

1 they can stick to synthetic DNA at 72 degrees. It can come in
2 and bind, and you can use that to make copies of this entire
3 piece.

4 So this is the modified probe. And down below in purple
5 is the amplicon.

6 Q. So does the amplicon include the universal priming site as
7 well as the complementary sequence to the target sequence?

8 A. Yeah. The universal priming site is on the outside. The
9 complementary sequence is on the bottom.

10 So if you flatten that out into the purple line, the --
11 you see those pieces on the ends and in the middle.

12 Q. So the amplicons in DANSR Version 2, can you make further
13 copies of the copies of the amplicons?

14 A. Sure. I could take this, and I could add it to a tube
15 with those primers -- right? -- independent of everything else,
16 and make many additional copies.

17 Q. So I think you have a prop of an amplicon?

18 A. I do. Actually, I have two. Grab this one (indicating)
19 and this one (indicating). Okay.

20 Q. So can you just explain what your prop is here?

21 A. Sure. So remember, the amplicons have pieces. This is
22 the piece down in the bottom that binds to the target sequence.

23 These are the handles. At the outside of the handles, you
24 have universal priming sites.

25 And actually here, in blue, is something called the

1 "Readout Cassette." And when we talk about the hybridizations
2 of the array, this is the piece that binds to the array.

3 Q. But just to be clear, when copies are made in DANSR
4 Version 2, it's made of the entire, entire piece there?

5 A. Right, it's made of the entire piece, end-to-end.

6 Q. Now, is -- is the amplicon ever bound to the microarray
7 that Illumina is pointing to as the second solid support?

8 A. No, the amplicon is not bound.

9 Q. What happens to the amplicon?

10 A. So we always talk about enzymes. In molecular biology,
11 we're always using proteins, enzymes from different species
12 like bacteria, and one of those is called a "restriction
13 enzyme." And when these are designed -- when the probes, the
14 outer probes are designed, restriction enzyme sites are put in,
15 so the enzyme can come in and actually cut the DNA; right? And
16 what it does is it cuts out this amplification, or, sorry, this
17 detection cassette.

18 So we started with this, which is the amplicon. We've now
19 cut out this piece.

20 Q. And what happens to the rest of the amplicon?

21 A. It gets washed away, just thrown away.

22 This is the piece that's used in the binding and detection
23 step.

24 Q. So we've been talking about -- a little bit about literal
25 infringement versus doctrine of equivalents.

1 A. Right.

2 Q. Is there any question here in your mind about whether
3 amplicons literally are immobilized to a second solid support
4 in Harmony™ Version 2?

5 A. No. This is an amplicon (indicating). This is not an
6 amplicon (indicating). This is what's immobilized to the array
7 (indicating).

8 And so there's no question at all.

9 Q. So what are some differences between the Readout Cassette
10 and the actual amplicon?

11 A. So this Readout Cassette -- right? -- is able to come in
12 very efficiently. It's small. It can move around very
13 efficiently. It comes in and binds very, very efficiently.

14 On the other hand, if you tried to bind a large piece of
15 DNA like this -- right? -- it comes in, flops around, maybe the
16 first piece will bind, but the second, and third, and fourth
17 piece, you have to bind a lot to eventually detect them. They
18 certainly run into each other, but they don't hybridize
19 efficiently.

20 And even Dr. Oliphant said they tried to use these, and
21 they simply wouldn't work. So they had to get rid of the idea
22 of using the amplicons and really focus in on using the Readout
23 Cassettes.

24 Q. Let's just be clear. Does the Readout Cassette include
25 the universal priming sites that's part of the amplicon?

1 A. Those have been cut off and thrown away.

2 Q. So can you actually make copies of the Readout Cassettes?

3 A. You can't copy these, no.

4 Q. And does the Readout Cassette contain the complementary
5 sequence that was on the amplicon?

6 A. No. The Readout Cassettes are actually designed to have
7 sequences which don't occur in the human genome, because you
8 don't want them to mess up and do other things.

9 Q. All right. Can you summarize -- well, let me ask you
10 this.

11 So Dr. Cooper also addressed something called "the
12 doctrine of equivalents" --

13 A. Yes.

14 Q. -- is that correct? And he offered his own personal view
15 that there are insubstantial differences between Readout
16 Cassette and an amplicon.

17 Do you agree with that?

18 A. No, I don't.

19 Q. And why is that?

20 A. I mean, these things are just very different.

21 The reason Ariosa chose to use the Readout Cassettes is
22 that these didn't work (indicating). These did (indicating).

23 And, in fact, using these gives you much better accuracy,
24 much higher quality results. That's what they were shooting
25 for when they chose these.

1 Q. And when you're saying "these," you're referring -- you're
2 holding the Readout Cassette?

3 A. I'm holding the Readout Cassette, yes.

4 Q. And in your view, are the differences between Readout
5 Cassettes and amplicons substantial or insubstantial?

6 A. They're substantial.

7 So we heard from Dr. Oliphant the Readout Cassettes work;
8 the amplicons don't.

9 Q. Okay. So could you summarize your non-infringement
10 opinion with respect to Element F for Version 2 of the Harmony™
11 assay?

12 A. Sure. The amplicons themselves are not immobilized, only
13 the Readout -- they're destroyed after applying restriction
14 enzymes. Only these Readout Cassettes are immobilized.

15 So Claim 1F is not practiced by Harmony™ Version 2.

16 Q. And if you could sum up your non-infringement opinions for
17 the '794 patent.

18 A. Sure. Neither Claims L, A and B are practiced in the
19 Ariosa Harmony™ tests. And Claim F is not practiced by
20 Harmony™ Version 2, so the Ariosa products don't infringe.

21 Q. Now, were there even other ways for Ariosa to do this
22 hybridization process?

23 A. Sure. The very first hybridization process could use
24 different strategies to biotinylate things so you could
25 eventually use beads to pull them out of the solution. And one

1 of them is to use biotinylated probes rather than biotinylated
2 DNA.

3 Q. And were biotinylated probes commercially available?

4 A. Sure. There's a project -- it's not a project -- product
5 from Agilent called "SureSelect" that uses biotinylated probes.
6 And the SureSelect product was available since 2009.

7 Q. And have the SureSelect probes been used with cell-free
8 DNA?

9 A. They've been used with cell-free DNA in applications in
10 cancer, where you want to pull tumor cells or tumor DNA out of
11 the bloodstream; they've even been used in applications for
12 non-invasive prenatal tests.

13 Q. And so was that another alternative for both Version 1 and
14 Version 2?

15 A. Yes.

16 Q. Okay. So before we turn to the '430 patent, just a few
17 questions on licenses.

18 You heard some testimony from Dr. Cooper.

19 Did you study the license technology in license agreements
20 between Ariosa and the University of Louisville, between
21 Verinata and MGH, and then thirdly, between Stanford and
22 Verinata?

23 A. Yes, I did.

24 Q. And in your view, was the technology licensed in those
25 agreements -- those three agreements -- reasonably comparable

1 to the '794 and '430 patents?

2 **A.** Yes. They involved aneuploidy detection; they involve
3 maternal fetal DNA; and they involve multiplex assays.

4 **Q.** All right. So let's turn to the '430 patent.

5 **A.** Okay.

6 **Q.** What version of Harmony™ do plaintiffs accuse of
7 infringing the '430 patent?

8 **A.** Only Version 2.

9 **Q.** Okay.

10 **A.** I'm sorry. Only Version 1.
11 I'm putting my molecules away.

12 It's only Version 1.

13 **Q.** Is there any dispute about infringement of Version 2 of
14 the Harmony™ test?

15 **A.** No, there's no dispute whatsoever.

16 **Q.** Okay. What element of Version 2 are you going to -- what
17 element of the '430 patent are you going to focus on today?

18 **A.** So there's a lot of description in Claim 1 about using
19 reference chromosomes. And it's really sort of crystallized in
20 Claim 1F, which is determining the presence or absence of fetal
21 aneuploidy using sequence reads from a first chromosome and
22 sequence reads from a reference chromosome.

23 **Q.** Now, what component of Harmony™ Version 1 does Dr. Cooper
24 claim practices this Element F?

25 **A.** It's the algorithm called "FORTE" that Dr. Wang introduced

1 yesterday.

2 Q. And so what is FORTE?

3 A. So FORTE is an algorithm that takes as input data to
4 sequence reads that come from the sequencer, transforms them in
5 a variety of ways so that they're no longer recognizable, and
6 then uses Monte Carlo simulations and other mathematical models
7 to predict aneuploidy risk.

8 Q. Now, in your view does the FORTE algorithm determine the
9 presence or absence of aneuploidy using enumerated sequence
10 reads from a first chromosome, and enumerated sequence reads
11 from a reference chromosome?

12 A. No, it doesn't.

13 Q. Now, is Ariosa still using FORTE in Version 2 of Harmony™?

14 A. Yeah, the Version 2 assay still uses FORTE to make
15 estimates of aneuploidy risk.

16 Q. Now, is Ariosa generating any sequence reads anywhere in
17 the Harmony™ process in Version 2?

18 A. No, there are no sequence reads whatsoever in Version 2.
19 It's arrayed binding data, so there's no sequence, at all.

20 Q. So if Ariosa is still using FORTE in Version 2, how could
21 FORTE be using enumerated sequence reads to determine the
22 presence or absence of aneuploidy from a first chromosome and a
23 reference chromosome?

24 A. It doesn't use sequence reads.

25 And the fact that Version 2 can still run the same

1 algorithm and make the same kind of risk estimates really
2 underscores the fact that it's not using those sequence reads.

3 **Q.** Now, where does the '430 patent describe an algorithm like
4 FORTE?

5 **A.** It doesn't describe any algorithm at all.

6 **Q.** Okay. So let's take a step back again and talk about some
7 basic concepts of assessing aneuploidies.

8 What's sort of the basic idea?

9 **A.** All right. So it might sound like this is really easy to
10 find aneuploidy; right?

11 If you have a fetus, it's aneuploid if it has an extra
12 copy of one chromosome.

13 So the way that aneuploidy commonly was detected a number
14 of years ago was through a process called "amniocentesis." You
15 stick a needle in, you pull out amniotic fluid, and essentially
16 you look at the cells and count the chromosomes; right?

17 So I use Chromosome 22 and 21, because they're about the
18 same size. But you look at them and you count and you'd see
19 two copies of Chromosome 22, but three copies of Chromosome 21.
20 So you'd look at a 3-to-2 ratio and say: *Aha! We have an*
21 *aneuploid.*

22 **Q.** And could one analogize that process to the sequencing
23 context?

24 **A.** Sure. If we were to sequence these chromosomes --
25 right? -- you'd get sequence reads that hopefully would

1 correspond to how much DNA there was.

2 So we could look in this amniotic fluid and look at DNA,
3 and we'd expect to see three sequence reads from Chromosome 21
4 for every sequence read we'd have from Chromosome 22.

5 **Q.** So that makes it sound very easy.

6 Is it, in fact, easy to detect or assess for aneuploidy
7 using maternal blood samples?

8 **A.** It actually gets really hard once you add the maternal
9 DNA; right? Because the mother is going to have the typical
10 number of chromosomes: Two copies of Chromosome 21, two copies
11 of Chromosome 22. And then diluted in her bloodstream is going
12 to be the fetal DNA; right?

13 So it's not going to be the same size. You're going to
14 have a tiny, tiny little bit where there might be a small
15 imbalance. And when we add these two together, what we're
16 actually detecting is a mix of Chromosome 21 and 22 where, if
17 you actually stack these bars up, you can see the boundary has
18 moved a little bit; but, you know, looking at it from far away,
19 it's almost indistinguishable.

20 And this is a best-case scenario.

21 **Q.** Now, are there additional challenges to detecting
22 aneuploidy even beyond this dilution of the fetal cell-free
23 DNA?

24 **A.** Right. So Dr. Wang yesterday was talking about one of the
25 challenges in doing this, and that's noise that comes in the

1 experiments.

2 And what the noise does is it kind of blurs that boundary.
3 So it's not even looking like looking at a clean line. What
4 you'd have to do is understand that the noise is going to make
5 detecting where that edge is very, very difficult.

6 **Q.** Can you give us an example from your own teaching career
7 to help us understand the concept of noise?

8 **A.** Sure. May I get up?

9 **THE COURT:** Sure.

10 **THE WITNESS:** Okay. Thank you.

11 So I used to teach physics; and in the very first physics
12 class on the first day, I'd want to teach students about noise
13 and measuring noise. So what I would do is I'd do a very
14 simple experiment. I'd have a box of metal bars, and I'd have
15 a ruler. And I'd take -- reach into the box and pull out the
16 metal bar, and I'd take the ruler and pass it to the first
17 student. I'd say: All right. Measure that bar, write it
18 down, don't tell anyone, and pass it on to the next person, and
19 so on; right? And I'd have them all do that and then write
20 down their answers. And then I'd pass around the box, and
21 they'd throw their answers in. I'd get up at the board, and
22 I'd have them unfold the piece of paper; right? So I'd look at
23 the answers, and I'd write them down and say, all right, well,
24 what -- does everybody measure the same way? And the answer
25 was no.

1 And, in fact, if you look at what we call the
2 distribution -- right? -- what you'd see is something that
3 looks like this (indicating). It's what in science you'd call
4 a Gaussian curve or a normal distribution. People often call
5 it a bell curve. And you'd see there's some spread in the data
6 that represents that noise.

7 And there are two parameters we use to talk about this.
8 One is the mean, and the other -- I should have drawn this more
9 even -- but the other one is the standard, S-T-A-N-D-A-R-D.
10 deviation; right?

11 And so the mean represents the average in the data. The
12 standard deviation represents the spread. And if I used a
13 different ruler, if I had one that was only mapped or only
14 marked every inch instead of sort of a standard ruler, you can
15 imagine there's much more spread in the data.

16 So if I were to look at a different ruler, different
17 experiment, I might see -- well, I might see a very broad, flat
18 curve instead of this one, where the mean might be the same,
19 but the variation -- the standard deviation would be much
20 bigger.

21 **BY MR. HEINRICH**

22 **Q.** Now, can we use these mathematical models to make
23 predictions?

24 **A.** Right. You can make predictions; right?

25 So if you weren't in the room when I first did this

1 experiment, you walked in, I might reach into the box -- might
2 reach into the box and grab another bar -- right? -- or grab a
3 random bar. I would give it to you and I would ask you to
4 measure it. And if you measured it and you reported back and
5 said "well, the answer is kind of close to here" I'd say "well,
6 you know, I'd probably grab the same bar.

7 If the answer was out here (indicating), I'd be much less
8 confident that you had grabbed the same bar. And, in fact, if
9 I had students measure all the bars, I could look at the
10 distribution, and I might see another one was centered here
11 (indicating); right? So depending on where you land, and
12 depending on the flex of curves you generate by doing this
13 experiment, I could actually say how likely it is that you
14 found this, and how likely it is that you found that. And I'd
15 say you're much more likely to have found this (indicating),
16 than that (indicating). Right?

17 So you can identify the bars by making measurements and
18 taking into account error.

19 **Q.** So thank you very much.

20 **A.** Yes.

21 **Q.** What are some of the sources of noise and measurement
22 error in the sequencing context?

23 **A.** So, you know, sequencing is a counting experiment, and one
24 of the things we know is that when you count things --
25 right? -- even birds flying by your window, there's going to be

1 some variation in what different people count.

2 Sequencers make errors in counting. There are systematic
3 errors that come from the steps that are carried out in a
4 laboratory to do the assays. Different batches of reagents we
5 now know cause variation. Different temperatures, different
6 days. If I put the same sequence on a different sequencer, I'm
7 going to get different data. So there are lots and lots of
8 different sources.

9 **Q.** Now, what teachings does the '430 patent provide for
10 handling and dealing with this noise and measurement error in
11 sequencing?

12 **A.** They provide none whatsoever.

13 **Q.** Okay. So now let's turn back to FORTE.

14 **A.** Okay.

15 **Q.** Now, did Dr. Cooper suggest that FORTE determines
16 aneuploidy by taking a test chromosome and comparing it to
17 sequence reads from a reference chromosome?

18 **A.** Yes.

19 **Q.** And is that accurate?

20 **A.** That's not accurate, at all.

21 If it was, you couldn't use it for Harmony™ Version 2.

22 **Q.** So can you explain for us how FORTE actually works? Why
23 don't we start with the first step?

24 **A.** All right. So as Dr. Wang explained the other day, the
25 sequence reads come off the sequencer, and they're carried

1 through a series of quality control filters and normalization
2 filters. And the most important is this quantile
3 normalization, which takes the sequence reads and, by looking
4 at all of the samples, all 96 samples in that same run,
5 produces the quantile normalized data which is fundamentally
6 transformed.

7 **Q.** And what does FORTE then do with that transformed data?

8 **A.** So this transformed data then goes into an algorithm that
9 does what's called "Monte Carlo simulations." That's based on
10 measuring means and standard deviations from the data; it does
11 a Monte Carlo simulation, gets a distribution -- right? -- the
12 Monte Carlo simulation is like synthetic experiments, so it
13 sort of estimates the variations of the error, and then it uses
14 those error parameters to construct more bell curves; and then
15 uses those bell curves for a disomic model and a trisomic model
16 to say: Which curve gives us the best fit.

17 **Q.** Okay, so that was a lot. So let's take it in smaller
18 chunks.

19 **A.** All right.

20 **Q.** Now, Dr. Cooper mentioned a proportion in his testimony.

21 **A.** Right.

22 **Q.** Is the -- can you tell a risk of aneuploidy looking at
23 that proportion?

24 **A.** No, you can't.

25 **Q.** Is that proportion a comparison of enumerated sequence

1 reads from a first or test chromosome and enumerated sequence
2 reads from a reference chromosome?

3 **A.** No, it's not. If it was, it wouldn't work for Version 2.

4 **Q.** Okay. So you mentioned Monte Carlo simulations in your
5 answer.

6 Can you tell us what Monte Carlo simulation is?

7 **A.** Sure. I'm sorry. When you talk about work, it's like
8 minds, I get excited.

9 Monte Carlo simulation is a way of conducting synthetic
10 experiments to empirically estimate errors in measurements.

11 **Q.** And so what is the point of using these Monte Carlo
12 simulations in FORTE?

13 **A.** FORTE realizes that any measurement is going to be
14 imprecise; right? If I ran the same data on a different day,
15 I'd get different measurements. And so it tries to estimate
16 how variable it is to give a risk estimate of aneuploidy.

17 **Q.** So you mentioned a disomic model and a trisomic model
18 that's generated through these simulations.

19 Can you explain that?

20 **A.** Sure. Can I --

21 **Q.** Sure.

22 **A.** All right. So I'm going to give you another little
23 drawing, all right.

24 So remember we started out with this proportion
25 (indicating), and that proportion is these transformed sequence

1 reads from Chromosome 21, transformed sequence reads from
2 Chromosome 21, and then 13 and 18.

3 And then additional things are done. We look across -- or
4 the algorithm looks across all 96 women, and its subtracts out
5 the average, the mean; right? So this has now shifted towards
6 zero. And then this is really the starting point. But then
7 the Monte Carlo simulations start.

8 So the algorithm looks at the spread in the data, and it
9 makes a Gaussian curve of Chromosome 21. It makes a Gaussian
10 curve for Chromosomes 13 and 18. It looks at the proportions
11 for all of the women, and makes another Gaussian curve; and
12 then it looks at the fetal fraction, because that's important
13 for doing aneuploidy detection.

14 **Q.** What does the fetal fraction refer to?

15 **A.** So the fetal fraction is the amount of fetal DNA in the
16 background of the maternal DNA. So remember this is typically
17 about 10 percent; but there's some spread across all of the
18 women in the population.

19 **Q.** Okay. And then what does FORTE do with these
20 distributions?

21 **A.** So what a Monte Carlo simulation does is says, all right,
22 we're going to calculate this mean-centered value now many
23 times. So it reaches into this distribution and it picks out a
24 value for 21, then it reaches into this distribution and it
25 picks out values for 13 and 18, and it does this 10,000 times,

1 and that let's you draw yet another curve to estimate what a
2 disomic pregnancy might look like in terms of this proportion,
3 starting with the transformed data from this quantile
4 normalized data from that.

5 **Q.** And just to be clear, is the data that's using these
6 Monte Carlo simulations influenced by the data from all 96
7 samples?

8 **A.** Right. The average across all 96 samples comes in when
9 this is subtracted. And the values for all 96 women, in fact,
10 are important in the Monte Carlo simulations.

11 **Q.** Okay. So how is the disomic model constructed?

12 **A.** So the disomic model is constructed the way I just
13 described.

14 **Q.** And then the trisomic model?

15 **A.** So the trisomic modal is actually more sophisticated,
16 because we have to assume the fetal fraction is going to kind
17 of shift that boundary. So it reaches in and pulls out now
18 10,000 times data from Chromosome 21, from 13 and 18, from the
19 proportion, and from the fetal fraction, and calculates another
20 Gaussian model.

21 So at the end of the day, we can draw some Gaussian
22 curves, and then look at this starting point in comparison to
23 those Gaussian curves.

24 **Q.** All right. Does FORTE consider even additional
25 information?

1 You can have a seat again.

2 **A.** Okay. So FORTE also takes into account --

3 -- so FORTE also takes into account other data, including
4 clinical history. So if a woman has previously had an
5 aneuploid pregnancy, she's at greater risk.

6 Maternal age: Older women have greater risks than younger
7 women.

8 gestational age: So the longer the fetus is carried
9 influences the risk.

10 **Q.** All right. So why don't we take a look at how FORTE
11 brings all of this together.

12 Let's pull up Exhibit 1658, which is in evidence, and go
13 to page 13.

14 **A.** Okay.

15 (Document displayed.)

16 **BY MR. HEINRICH**

17 **Q.** And this is one of the FORTE presentations that Dr. Wang
18 testified about yesterday?

19 **A.** Yes.

20 **Q.** So what do we see here in this slide?

21 **A.** All right. So remember I told you there were Gaussian
22 curves that came out of this Monte Carlo 10,000 permutation
23 simulation?

24 The green curve is the disomic model.

25 The red curve looks like a flat line, but it's actually a

1 curve; right? The measurement is hard, so it gets squashed
2 down.

3 And the black line is the proportion that came from the
4 quantile normalized data for this individual.

5 **Q.** And so what likelihood does FORTE output for an example
6 like this?

7 **A.** So this is like the example I gave you earlier with two
8 metal bars. They're asking what's more likely: The disomic
9 model green curve or the trisomic model, the red curve.

10 And the easiest way to think about this is if you look at
11 that black line coming down, it hits the green curve first --
12 right? -- so it's more likely that this is a disomic pregnancy.

13 **Q.** So if we think about bell curves --

14 **A.** Right.

15 **Q.** -- and we sometimes talk about outliers in a bell curve,
16 would this actually -- this observed data actually be on the
17 outlier of the disomic model?

18 **A.** Right. Yeah, I mean, in any population you're going to
19 have people that are outliers; right?

20 Even all disomic pregnancies are going to have outliers
21 when you do this assay.

22 So this would be an outlier. It's toward the end of the
23 curve. But the sophistication of building in the trisomic
24 model actually allows them to make a better estimate than the
25 estimate that this is. Even though it's near the end, it's

1 still more likely to be disomic.

2 **Q.** All right. So let's go to the next slide.

3 What's changed in this example from the previous slide?

4 **A.** So if you look at the top -- and this is really
5 interesting. This is exactly the same input data in terms of
6 the data that came out of the sequencer, went through all of
7 these steps. So same -- it has the same standard deviation,
8 the same F.P. -- that's the fetal fraction, how much fetal DNA
9 is there. The only difference is the maternal age has changed.

10 **MR. REINES:** Your Honor, this is not in his report,
11 so I would object to it.

12 **MR. HEINRICH:** Well, he considers this as a document
13 that's cited in his report. It's in his list of materials
14 considered, and he goes through great detail on how FORTE works
15 with the Monte Carlo simulations, Your Honor.

16 **MR. REINES:** That has nothing to do with the opinion
17 that's being based on this Struble document.

18 **THE COURT:** This document, though, was referenced in
19 the report?

20 **MR. HEINRICH:** Yes.

21 **MR. REINES:** But the opinion regarding maternal age
22 wasn't.

23 **THE COURT:** Okay. Overruled. You may proceed.

24 **BY MR. HEINRICH**

25 **Q.** Okay. So if you can continue?

1 A. Sure. So could you toggle back and forth between this
2 slide; right.

3 So this one is maternal age of 20. If you look down here
4 in the lower right corner, this is maternal age.

5 Toggle forward.

6 This is maternal age at 40. You can see that curve moves
7 up a little bit. And now if you look where the black line
8 comes down and hits the curve, it actually hits right at the
9 point where the red curve and green curve come together.

10 And so the estimate here is there's actually a 50/50
11 chance of aneuploidy.

12 Q. Now, do any of the red, green or black lines here
13 represent enumerated sequence reads from a first or test
14 chromosome?

15 A. No, they don't.

16 Q. Do any of them represent enumerated sequence reads from a
17 reference chromosome?

18 A. No.

19 Q. Does FORTE determine the presence or absence of aneuploidy
20 using enumerated sequence reads from a first chromosome and
21 enumerated sequence reads from a reference chromosome?

22 A. No, it doesn't.

23 Q. Does FORTE determine the presence or absence of aneuploidy
24 at all?

25 A. No, it determines risk for aneuploidy, which, you know,

1 honestly is a much more faithful way of representing what's in
2 the data.

3 **Q.** So can you provide us a summary of your opinion on the
4 '430 patent?

5 **A.** Sure. If we look at '430, Claim 1, Element F, it requires
6 the use of a test in reference chromosomes or sequence reads
7 from those tests and reference chromosomes to determine
8 aneuploidy.

9 And I hope it's clear that FORTE simply doesn't do that.

10 **MR. HEINRICH:** Okay. Thank you very much.

11 **THE COURT:** Mr. Reines.

12 **MR. REINES:** Thank you very much, Your Honor.

13 (Whereupon a document was tendered to the Court.)

14 **THE CLERK:** Oh.

15 **THE COURT:** Thank you.

16 **CROSS-EXAMINATION**

17 **BY MR. REINES**

18 **Q.** All right. Let's everybody get settled.

19 Okay. Thank you.

20 Dr. Quackenbush, do you recall on direct exam you stated
21 that you thought that the difference between performing Step A
22 of Claim 1 of the '794 patent, that that was a significant
23 difference.

24 Do you recall that testimony, generally?

25 **A.** The performance of Step A and B?

1 Q. Yeah, the sequence.

2 A. I'm sorry. Which patent?

3 Q. The '794 patent. Like I said, Claim 1 of the '794 patent,
4 do you recall saying that the sequence of Step A and Step B,
5 that you thought it was significant which one was performed in
6 which order?

7 A. Yes, that's what I said this morning, too.

8 Q. That's all I wanted to clarify.

9 I'd like to direct your attention to the testimony of
10 Dr. David Ward, dated March 12th, 2015, at page 164, which
11 should be open right in front of you.

12 A. All right.

13 Q. At line 5, through page 165, line 12.

14 And Dr. Ward was --

15 MR. HEINRICH: Excuse me. Could you give me the page
16 and line numbers again?

17 MR. REINES: Sure. Of course. 164, line 5 through
18 165, line 12.

19 Q. And you understand Dr. Ward was an expert retained by
20 Ariosa for its '794 patent?

21 A. I'll assume that's correct. I don't recall.

22 Q. Okay. The question was:

23 "Could you explain what was the basis of your
24 testimony that it didn't matter whether you did Step
25 A first or Step B first of Claim 1 of the '794

1 patent?"

2 That was the question.

3 And Ariosa's expert -- not you, but the other one that's
4 not here -- the answer was I said --

5 **MR. HEINRICH:** Objection. This is getting into some
6 claim construction issues that the Court resolved.

7 **MR. REINES:** Your Honor, this --

8 **THE COURT:** I don't even have this. Where are you
9 reading it?

10 **MR. REINES:** Oh, I think it was handed up.
11 (Whereupon a document was tendered to the Court.)

12 **MR. REINES:** I'm sorry. Here you go.

13 **THE CLERK:** Oh, I'm sorry.

14 **MR. REINES:** No, that was my fault.

15 **THE CLERK:** There we go.

16 **MR. HEINRICH:** I believe that Your Honor excluded
17 this, because this goes to the order of steps issue that was
18 resolved.

19 **MR. REINES:** Your Honor, he testified that it was
20 significant technologically that Step 1 and Step 2 were the
21 order of steps. This is responding directly to that.

22 It can't be that we can't establish that their other
23 expert said the opposite.

24 **MR. HEINRICH:** There is no doctrine of equivalents
25 issue with this -- with these two elements.

1 **MR. REINES:** But they opened the issue.

2 **THE COURT:** You know, you folks are arguing more than
3 you should in this context.

4 **MR. REINES:** Understood. But he clearly gave that
5 testimony.

6 **THE COURT:** I'll tell you what. It's early, ladies
7 and gentlemen, but we're going to take our morning recess at
8 this time. If you'd be ready to come back, please, at quarter
9 until 10:00.

10 In the meantime, don't discuss this matter with each other
11 or anyone else, or make up your minds. You have not heard all
12 of the evidence yet.

13 (Proceedings were heard outside the presence of the jury:)

14 **THE COURT:** Okay. Now where are you looking?

15 **MR. REINES:** This is at 164, line 5 through 165, line
16 12.

17 **THE COURT:** This depo was in?

18 **MR. REINES:** 2015.

19 **THE COURT:** 2015.

20 **MR. REINES:** I think the key issue, Your Honor, is
21 that on direct, Dr. Quackenbush said that there was a
22 significant difference technologically between doing A before B
23 and B before A. That was clearly interjected. We have to be
24 able to demonstrate, because he was talking about --

25 **THE COURT:** I know. I just haven't read this yet.

1 **MR. REINES:** Fair enough. Sorry.

2 (Pause in proceedings.)

3 **MR. HEINRICH:** So this is a --

4 **THE COURT:** He doesn't say things so different from
5 what this witness has said, but...

6 **MR. HEINRICH:** This is testimony from the IPR that
7 they proffered this in support of their claim construction
8 argument: The order of steps doesn't matter.

9 The Court ruled in docket number 547 the Court would
10 exclude IPR testimony if it relates solely to the order of
11 steps A and B. That's what this is.

12 Dr. Quackenbush didn't open the door to anything. He
13 simply said that this was an important difference. Saying
14 there's an important difference can't possibly open the door to
15 evidence that would only possibly relate to DOE, which doesn't
16 apply to these claim steps.

17 **THE COURT:** Where did you read from what I said?

18 **MR. HEINRICH:** This is docket number 547 at page 6.

19 **THE COURT:** (Reading)

20 "As a preliminary matter, the Court excludes any
21 testimony from the post grant proceedings regardless
22 of whether it's hearsay if it relates solely to the
23 order of steps A and B."
24 the Court already decided that.

25 **MR. REINES:** Your Honor, they argued that it's much

1 more.

2 **THE COURT:** (Reading)

3 "To the extent the parties believe the related
4 testimony is relevant to another issue, they shall
5 request specific relief prior to presenting such
6 testimony."

7 So you think this is related to another issue which is
8 Whether it's -- whether it matters?

9 **MR. REINES:** Whether it's much more efficient --
10 which remember that they're all banging around, which goes to
11 the 100 issue.

12 The argument that was being made is that it's much
13 efficient to put it -- have them floating around, I think, and
14 instead of already attached to the beads at the time.

15 **THE COURT:** Right.

16 **MR. REINES:** And that relates to the one hundred
17 issue, which is what's the rate that this gets accomplished.

18 And I think the point that was being made is: It's just
19 way better to have them in the solution without the beads in
20 and hold the beads for later.

21 It also goes to the credibility of what was the purpose of
22 the change. Was the waiting two hours to put the beads in an
23 attempt to create another non-infringement argument, which it
24 obviously was, or was it actually to make an improved test,
25 which it wasn't.

1 So it goes to willfulness. It goes to the 100 issue. It
2 goes to the credibility of the witness.

3 I mean, what doesn't it go to? It goes to numerous
4 issues.

5 And he specifically -- I mean, he specifically said -- I'm
6 not even sure if it was in his report, so I was a little -- you
7 know, it just happened that it's much more efficient, it gives
8 you a better result, because you can have the molecules moving
9 around, and they can more easily find each other. That's this
10 hotly contested 100.

11 **THE COURT:** He says that in here. He says that in
12 here.

13 **MR. REINES:** He says: In the real world, and not in
14 my hands, that is what I said I would have said, in my hands
15 there's not a significant difference.

16 **THE COURT:** Then he says: (Reading)

17 "There is one possible benefit, and that is by
18 putting the molecules onto a surface that you
19 increase the kinetics of the reaction by reducing the
20 complexity."

21 And, I mean, that's essentially what he was saying.

22 **MR. REINES:** No, that's the opposite. That's on the
23 surface.

24 **THE COURT:** On the surface. And, okay, I'll read the
25 rest of it then. (Reading)

1 Or you add the probe and 10 seconds later you add or,
2 blah, blah, over time, that's the only advantage.
3 Because the one difference is that if you add a lot
4 of probes to the sample first, then you're doing a
5 solution hybridization.
6 And if you add the capture thing, you're doing --"

7 **MR. REINES:** Tends to give you better kinetics. It's
8 the opposite of what he said. And it proves the 100 point. It
9 proves the credibility point. It proves the willfulness point
10 strongly.

11 **THE COURT:** Oh, better kinetics, I see, on the hard
12 surface, on the solid surface, than not.

13 Is that what you want to read this for?

14 **MR. REINES:** Yes. And then the final paragraph where
15 he says:

16 "In my hands there's no significant difference
17 between which way you do it," which goes to the
18 kinetics point.

19 Well, I mean, if anything, it just helps us on the
20 kinetics, which is fine. I'll take that, alone.

21 **THE COURT:** All right. Well, I'll allow it for that.

22 So what shall I tell them 10:00 till --

23 (Discussion held off the record.)

24 (Recess taken from 9:40 a.m. until 9:50 a.m.)

25 (Proceedings were heard in the presence of the jury:)

1 **THE COURT:** And you're still under oath from before,
2 sir.

3 **THE WITNESS:** Thank you.

4 **MR. REINES:** Thank you, Your Honor.

5 **Q.** The question that was posed to Ariosa's expert was:
6 "Could you explain what was the basis of your
7 testimony that it didn't matter whether you did
8 Step A first or Step B first, of Claim 1 of the '794
9 patent?"
10 And Ariosa's expert responded:
11 "The reason why I said that was I believed that what
12 I said is that if you have a sample, and you were
13 going to target multiple, or you were going to try to
14 detect multiple targets, you can add the oligo or the
15 probe to that mixture.
16 "And then given that, you have a way of collecting
17 this or separating your specific target molecules
18 from the rest. There's not a significant difference
19 in both approaches.
20 "There is one possible benefit of doing A before B,
21 and that is by putting the molecules onto a surface,
22 that you increase the kinetics of the reaction by
23 reducing the complexity. But if you do those
24 simultaneously, or you add the probe, and then 10
25 seconds later or five minutes later you add the first

1 solid phase selector, the only advantage I see,
2 because you can't do it -- you can do either one.
3 I want to make sure I got that.

4 "That's the only advantage I see, because you can do
5 either one.

6 "Because the one difference is that if you add probes
7 to the sample first, then you're doing a solution
8 hybridization. If you add the captured thing, you're
9 doing capturing the thing, and your hybridization, if
10 it's added after it's being done on a solid surface,
11 which tends to usually give you better kinetics.

12 "But I've done them both ways in real life, and
13 there's not -- in my hands -- and this is why I said
14 what I said -- in my hands there's not a significant
15 difference."

16 All right. I'd like to ask you about Version 1 of
17 Harmony™.

18 Oh, actually, before I do that, did you know Dr. Cantor,
19 who is going to be the next expert for Ariosa? Did you know he
20 shared Dr. Ward's opinion on that topic?

21 **MR. HEINRICH:** Objection. Objection. Counsel is
22 testifying. He's making --

23 **MR. REINES:** I'm asking if he knows. I have a
24 foundation for it.

25 **THE COURT:** I'll sustain the objection. You need to

1 reframe it.

2 **BY MR. REINES**

3 **Q.** Okay. Are you aware of what Dr. Cantor's testimony is on
4 the question of the significance of the difference between
5 whether you do it on solid phase, whether you have the solid
6 phase first, or you do the solution hybridization?

7 **A.** Off the top of my head, no.

8 **Q.** All right. Let's get in to Version 1 of Harmony™. And
9 there, your non-infringement argument is based on this issue of
10 the sequence of Step 1 and 2; correct?

11 **A.** That's what the Court has told us we should consider, sir,
12 yes.

13 **Q.** Okay. And with respect to that, let's look at the
14 Standard Operating Procedure documents; Standard Operating
15 Procedure document -- that's Ariosa's document. That's
16 Exhibit 55, and it's been admitted already.

17 **A.** Okay. Can I find it, please?

18 **MR. REINES:** Of course.

19 (Document displayed.)

20 **THE COURT:** While he's doing that, ladies and
21 gentlemen, I'll mention people have alluded several times in
22 the course of this trial to things the Court has said about
23 what these patents mean. And what they're referring to is that
24 there are all kinds of procedures we go through before we reach
25 the point where we submit these questions to a jury. And one

1 of the procedures that we go through is that if the parties
2 dispute what a particular term means or a particular word means
3 in context, then they bring that dispute to the Court, and the
4 Court will answer and will say: All right. It means this...

5 So when they've been talking about A before B just now,
6 the Court said, as the witness just said, the Court said: "All
7 right. A has to go first, and B has to go second."

8 So that's what they're referring to, is some explication
9 type orders that have been issued prior to the time you got
10 here today.

11 **MR. REINES:** Thank you, Your Honor.

12 **Q.** Exhibit 55, page 2, and specifically 7.4?

13 **A.** Okay.

14 **Q.** And if we can get that up on the screen, and let's
15 highlight where it says that "is immobilized onto"-- and then
16 it says, "DynaL MyOne Streptavidin-coated magnetic beads."

17 **MR. GINDLER:** Not a confidential document.

18 **BY MR. REINES**

19 **Q.** Do you see that in front of you?

20 **A.** I see what you highlighted.

21 Can I read the passage, please?

22 **MR. REINES:** Of course.

23 **THE WITNESS:** Okay.

24 **BY MR. REINES**

25 **Q.** And so that's stating that the step that the Standard

1 Operating Procedure of Ariosa's own documents states is that
2 you're attaching the single-stranded DNA to the solid support;
3 correct?

4 **A.** No. If you look at the entire section -- right? -- the
5 section is entitled "background and test principles."

6 So this is describing the general principle of the assay;
7 right? You're trying to explain why you're doing things;
8 right? So this isn't the actual series of steps that's being
9 carried out; it's teaching the people who are going to do the
10 assay why you're doing things.

11 And so the telling --

12 **MR. REINES:** Your Honor, I'd ask that this be
13 confined to yes or no. I just asked him whether it showed
14 that.

15 **THE COURT:** No, he's answering your question. So you
16 may finish.

17 **THE WITNESS:** Right. So what that is showing is why
18 you attach the biotin, as I said earlier. It's not showing
19 that that's what's happened.

20 **BY MR. REINES**

21 **Q.** So this isn't stating that the single-stranded DNA is
22 being attached to the bead?

23 **A.** No, it's telling you why you attach the biotin.

24 **Q.** All right. And then the next sentence states:

25 "Trios of DANSR oligos specific for each of the

1 selected loci are then annealed to the immobilized
2 DNA."

3 Do you see that?

4 **A.** I see that, yes.

5 **Q.** Okay. And let's look at the figure that's shown in the
6 Standard Operating Procedure, Ariosa's own document showing how
7 it's performed.

8 (Document displayed.)

9 **BY MR. REINES**

10 **Q.** And you see that, first -- I'm just going to ask you what
11 the items are: That there's a single-stranded DNA not attached
12 to anything, at the top right column.

13 Do you see that?

14 **A.** I see what you're highlighting, yes.

15 **Q.** And then the next thing that's shown immediately under
16 that is that the single-stranded DNA is attached to the bead;
17 correct?

18 **A.** I see a figure that you're describing that way, but it's
19 not the protocol that's being used.

20 **Q.** Okay. And then the next figure down, after that, shows
21 that the Streptavidin bead has the single-stranded DNA; and
22 that's where the probes are, in the third item?

23 **A.** You're describing what's in the cartoon, yes.

24 **Q.** Okay. And your argument that you tendered to the jury is
25 that in the Standard Operating Procedure of Ariosa's own

1 product documentation, when it's showing this step by step,
2 going down -- that's not actually the order of steps, that's
3 just to explain what's happening; is that correct?

4 **A.** This is in the section called -- so it's called background
5 and test principles; right?

6 **Q.** Okay.

7 **A.** You're explaining why and how the general reaction is
8 going to be carried out. It's not telling me -- it's not
9 telling you the operating procedure that's later on in the
10 document.

11 **Q.** I think your argument is clear.

12 If we now turn to Exhibit 561.

13 And with respect to 561, if you could please turn to page
14 14.

15 Do you have that in front of you?

16 **A.** Sure.

17 **Q.** Okay. And this is one of those interrogatory responses;
18 correct?

19 Do you know what an interrogatory response is?

20 **A.** Yes, I'm trying to find out what exactly it is.

21 Yes, I see that.

22 **Q.** Okay.

23 **MR. HEINRICH:** Objection. This is not in evidence, I
24 don't believe. And this is an interrogatory response, so it
25 can be read in, but not --

1 **THE COURT:** Did you put this on the screen?

2 **MR. REINES:** I guess it's up, yes.

3 **THE COURT:** Don't put it on the screen yet.

4 **MR. REINES:** Okay. Your Honor, the situation is this
5 is their corporate answer as to the order of steps, and it
6 shows the figure. So there's really no way for me to read it
7 in.

8 **THE COURT:** All right. Hang on.

9 **MR. REINES:** Since they're --

10 **THE COURT:** This is question number five, is what
11 you're on?

12 **MR. REINES:** Yes, at page 14, line 7.

13 **THE COURT:** Well, it starts at page 12.

14 **MR. REINES:** Right. But the figure is --

15 **THE COURT:** But the response starts at page 13 and
16 goes to page 16.

17 **MR. REINES:** Right. On page 14 is the relevant
18 portion, which shows the figure that we just looked at. And
19 Ariosa explains as its corporate answer that that shows the
20 order of steps, or the steps I should say.

21 You see at line 7, it says, "The figure immediately below
22 describes it's an --"

23 **MR. HEINRICH:** Objection. Objection.

24 **MR. REINES:** It's an interrogatory response,
25 Your Honor.

1 **THE COURT:** And --

2 **MR. REINES:** This isn't privileged information. This
3 is their corporate response.

4 **THE COURT:** Please don't argue.

5 **MR. REINES:** Okay.

6 It also looks just like the last exhibit.

7 **MR. REINES:** I'll refer to it that way.

8 But can I introduce the sentence immediately above it that
9 tells what it is?

10 **THE COURT:** Yes.

11 **MR. REINES:** Okay. Thank you, Your Honor.

12 **MR. HEINRICH:** We would ask that the whole response
13 be read so that it's not taken out of context.

14 **MR. REINES:** Your Honor, they can -- they can ask
15 about that.

16 **THE COURT:** It's getting -- what's happening now,
17 ladies and gentlemen, as I told you when we first picked you as
18 jurors, we're going to try to be respectful of your time, and
19 one way we do that is we give people time limits. They're
20 starting to run out of time, so you may have noticed an
21 increasing testiness about the behavior of the lawyers and the
22 witnesses. That's because they're short on time. So now
23 they're fussing about who needs to get the rest of this in, and
24 whose time it should be on.

25 Like so much else in these cases, the questions are long,

1 and the answers are longer. So it will take a lot of time.

2 So at this point I will allow you just to show the lines 7
3 through 20 that you wanted to.

4 **MR. REINES:** Thank you, Your Honor.

5 (Document displayed.)

6 **MR. REINES:** Can you put that up on the screen,
7 please, just 7 through 20.

8 **Q.** Okay. Do you see immediately above the exact same figure
9 showing the single-stranded DNA alone up on top on the right
10 that says:

11 "The figure immediately below describes schematically
12 the steps of the DANSR assay."

13 **A.** I see where it says that, yes. And I think the word
14 "schematically" is -- I think it's important, because it shows
15 the general principles, as I told you earlier when I looked at
16 the SOP. It's not the background section.

17 **Q.** Right. And your argument is this isn't showing an order
18 of steps; right?

19 **A.** This is a teaching tool.

20 **Q.** Okay.

21 **A.** It's not truth. It's not the way the steps are performed
22 in the assay.

23 **Q.** And you rely on the exact same diagram when it showed that
24 the probes were binding first; and then the -- then the duplex
25 was being attached to the probe on -- on the SOP for Version 2;

1 you relied on that in your examination?

2 **A.** I didn't rely on that. I relied -- I used that, again, as
3 a teaching tool.

4 What I relied on is the order of steps provided in the
5 SOP.

6 What we know happens, we read about the steps where things
7 were added in the laboratory; I looked at the steps where we
8 added the thermocycler. I mean, all of those were important.
9 I used it as a teaching tool the same way that's it used as a
10 teaching tool in the SOP one.

11 **Q.** All right. I'd like to turn to the Streptavidin/biotin
12 attachment strength.

13 **A.** Mm-hm.

14 **Q.** Now, when things are placed in the Streptavidin/biotin
15 bond is something that occurs in the context of where the bead
16 and the single-stranded DNA connect; is that correct?

17 **A.** So --

18 **Q.** Or the DNA?

19 **A.** Or the DNA attaches, yes.

20 **MR. REINES:** I'll try to be less testy, Your Honor.

21 **Q.** And you understand that that connection between the bead
22 and the DNA through biotin is the strongest non-covalent
23 biological interaction known?

24 **A.** That's why that Streptavidin/biotin reaction is used, yes.

25 **Q.** And you understand that this association constant is on

1 the order of 10 to 15?

2 A. Right. It's a very strong bond.

3 Q. Now, I believe you relied on some testimony from Dr. Fan.
4 Is that something that you considered in your opinion,
5 regarding the order of steps that would likely happen in a
6 mixture?

7 A. I read his deposition, yes.

8 Q. Okay. And do you know whether that was about DNA at all?

9 A. I'd have to go back and look in context, but I believe it
10 was about DNA. He was talking about hybridization. So, yes,
11 it involved DNA.

12 Q. Do you recall that was from the '810 application where
13 they're talking about RNA?

14 A. I'd have to go back and look at it.

15 RNA is a molecule. Like DNA, it has a series of bases.
16 The difference is the sugar phosphate backbone is ribose
17 instead of deoxyribose; but it has the same base pairing rules,
18 and the kinetics are exactly the same.

19 Q. And in there, the connection that was being made wasn't --
20 didn't involve Streptavidin at all?

21 A. I'd have to go back and look.

22 Q. Okay. You don't know? Do you remember?

23 A. Off the top of my head I don't recall.

24 Q. Okay. Very good.

25 All right. Let's talk about the 100 issue and how much of

1 the -- how much is actually attached between the hybridization
2 of the probes to the single-stranded DNA, before and after?

3 A. I'm sorry. I don't understand what the 100 issue is.

4 Q. Okay. I'll start again.

5 Do you know that there's a requirement in the claim that
6 relates to the term -- to 100?

7 A. I think that you have to provide a hundred single-stranded
8 targets or something.

9 Q. Do you know about that?

10 A. I can read the claim language. I don't recall the exact
11 wording, but I remember the number 100 appeared.

12 Q. This doesn't come up in your direct examination --
13 right? -- the 100 issue?

14 A. We didn't talk about a hundred, no.

15 Q. Very good.

16 All right. Now, let's talk about how much DNA would bond
17 between the bead and the single-stranded DNA versus the
18 hybridization of the probe to the single-stranded DNA. That's
19 one of the issues I do believe you did address that.

20 A. Right.

21 Q. Okay. With respect to that, do you know Ariosa's
22 corporate representative regarding the DANSR assay specifics,
23 Jacob Zahn? Did you rely on him.

24 A. I don't know him personally.

25 Q. You relied on him for purposes of your opinion; correct?

1 A. I wouldn't say relied on; right. I read all of these
2 documents, and based on evaluating many different aspects of
3 what people were presenting, I arrived at what I thought was an
4 informed scientific conclusion.

5 Q. Did you rely on the testimony at all? You did or
6 didn't -- it's your choice -- of Dr. Jacob Zahn, who was
7 Ariosa's corporate representative regarding the specifics of
8 the biochemistry in the DANSR assay?

9 A. I considered it.

10 Q. Okay. Did you rely on it?

11 A. I'm not going to say I relied on it. I synthesized
12 information from lots of documents.

13 Q. All right. Do you know that Dr. Zahn testified that all
14 he could say was that the vast majority of the single-stranded
15 DNA was hybridized before the DNA was attached to the beads?
16 All he could say was vast majority?

17 A. He may have said that.

18 Q. Does that sound familiar to you?

19 A. I assume that's what he -- I'll give you the benefit of
20 the doubt on this one, that is what he said, yes.

21 Q. Okay. All right. Let's turn to the question of
22 amplicons, and specifically Exhibit 422, which is the Standard
23 Operating Procedure of Ariosa.

24 And let me know when you have that. I want to make sure
25 you have it in front of you.

1 A. Okay. So I have 422 open.

2 Q. Great.

3 (Document displayed.)

4 BY MR. REINES

5 Q. And it's in front of me. If we could just highlight the
6 purpose, please.

7 And according to you, these Standard Operating Procedure
8 documents from Ariosa that all of the experts have been relying
9 on, those are teaching? They teach you about what's actually
10 taking place; is that right?

11 A. They tell you about what's going to be performed in the
12 lab, yes.

13 Q. They tell you -- they tell you about what's going to be
14 performed in the lab; is that right?

15 A. Yes.

16 Q. Okay. Now, it states in the purpose:

17 "To establish the procedure by which purified PCR
18 amplified product is transferred and consolidated
19 into a 384 well plates and hybridized to the array of
20 pegs."

21 Do you see that?

22 A. Yes, I do.

23 Q. And the purified PCR amplified product -- the amplified
24 product is what you're calling the cassette that you had with
25 that prop?

1 A. So what's hybridized to the array is the cassette, yes.

2 But what it says here is something more general; right?

3 It's the procedure by which purified amplified product --

4 right? -- so I don't know what they're considering here. I

5 don't know if they are considering this to be amplicon or the

6 product; right? There's vagary here, and I don't know if they

7 wrote this considering the definition of "amplicon" that we're

8 using right now.

9 Q. Well, let's be -- I'm sorry?

10 A. The cassettes, you know, are a product of the PCR. But

11 given the definition of amplicon that we have, they're no

12 longer that amplicon.

13 Q. And what's the definition that you're applying that makes

14 you say that?

15 A. Well, if you remember, the Court's claim construction

16 tells us that the amplicons are the amplified products that

17 come from copying the modified probes; and the modified probes

18 have those universal priming sites we talked about, and a

19 section which can hybridize to the target sequence; right?

20 And those amplicons -- sorry -- the Readout Cassettes

21 can't hybridize to the target sequence, and don't have those

22 priming sites.

23 Q. And when it refers to purified PCR amplified product as

24 the purpose for the Standard Operating Procedure in describing

25 DANSR, and then it -- it says here that that amplified product

1 is hybridized to the array of pegs -- do you see that?

2 A. If you take the amplicons --

3 Q. Please answer my question.

4 A. I see that, yes.

5 Q. Okay. And so my question to you is: What you're saying
6 is when it says, "purified PCR amplified product," you just
7 don't know what that is in the process?

8 A. No. What I would say is that when you take the
9 amplicons -- right? -- this is a long protocol, so you do many
10 things. And the input is going to be the amplicons; right? I
11 agree with that. But then you treat them with additional
12 enzymes to make the product; the Readout Cassette that's
13 hybridized to the array. Right?

14 So this doesn't say take the amplicons and throw them on
15 the array. It says take the PCR amplified product; right? And
16 that product is what comes from applying the series of steps
17 with restriction.

18 Q. So you're acknowledging that the purified PCR amplified
19 product there is the cassette; right? That was my original
20 question.

21 A. I would have to read this entire thing to decide what
22 exactly they're -- or understand exactly what they're referring
23 to. What's applied to the array is the cassette.

24 Q. And this document is one of the central documents you're
25 relying on for your opinions in this case?

1 A. Again, I wouldn't say I relied on any document.

2 I considered all of these documents to try to arrive at an
3 informed opinion.

4 Q. So is there any one document in this whole case that you
5 can say you're relying on for your opinion?

6 A. I will say I considered many, many different documents
7 in -- in coming to my opinion.

8 Q. Is there any document you'll acknowledge that you relied
9 upon?

10 A. I have considered many and relied on them.

11 Q. So you won't just acknowledge that you relied on any
12 document?

13 A. I don't know what you're asking me. I considered many,
14 many different documents.

15 Q. All right. I'd like to ask you -- I'd like to read the
16 Court's claim construction in, so that we have that --

17 A. Mm-hm.

18 Q. -- on this issue, so that we're a little more precise.

19 It says:

20 "The court construes wherein said different modified
21 probes are amplified and forming different amplicons,
22 to mean where the wherein the different modified
23 probes are replicated in whole or in part to yield
24 amplification products of each of the different
25 modified probes."

1 Does that sound like the -- the definition you were
2 supposed to apply?

3 **A.** I'll agree that is the first part of the definition, which
4 I showed earlier.

5 **Q.** You don't have a problem with that definition; right?

6 **A.** Um.

7 **MS. HABERNY:** It's not allowed.

8 **THE WITNESS:** I want to stay out of trouble.

9 **MR. REINES:** I know that.

10 **Q.** All right. I want to ask you a question about the '794
11 patent in Claim 2.

12 You evaluated Claim 2; correct?

13 **A.** Yes. Can I open it up, please?

14 **Q.** Please.

15 **A.** Can you tell me the document numbering?

16 **Q.** My bad. 514.

17 **MS. JONES:** 513.

18 **MR. GINDLER:** 13.

19 **MR. REINES:** Thank you, Mr. Gindler.

20 **Q.** And if you have that at Claim 2.

21 (Document displayed.)

22 **BY MR. REINES**

23 **A.** It's easier to read up here. It's right here.

24 **Q.** All right. Thank you.

25 All right. And you understand Claim 2, and that this is

1 one of the -- the claims that you had to analyze for your
2 infringement position?

3 **A.** It's one of the ones I had to analyze, yes.

4 **Q.** Okay. And in terms of the Claim 2, it uses the term
5 "detection position."

6 Do you see that?

7 **A.** Yes.

8 **Q.** And that refers to a single base; correct?

9 **A.** It doesn't -- I mean, I'm not sure what the definition
10 here is in terms of detection position.

11 **Q.** But your understanding of the patent -- because you needed
12 to understand Claim 2 for your opinion -- is that it refers to
13 a single base; correct?

14 **A.** I'm not sure what it refers to. I'd have to go back and
15 read the patent more completely.

16 For the purposes of today, I really focused on Claim 1,
17 because there would be no infringement of Claim 2 if Claim 1
18 isn't infringed.

19 **Q.** All right. I'd like to play your deposition from your
20 August 15th, 2017, deposition at 158, line 13, through line 25.

21 **THE WITNESS:** Okay. Thank you.

22 **MR. REINES:** All right. Let's play it, please.

23 (Videotape was played but not reported.)

24 **BY MR. REINES**

25 **Q.** Now, with respect to the '794 patent, one more question,

1 which is your understanding of the '794 patent -- that does not
2 pertain to sequencers; right?

3 **A.** In the Abstract, no, it doesn't pertain too sequencers.

4 But in the context of the argument that you've been
5 presenting, sequencing is detection.

6 So when the '794 patent is filed, sequencers hadn't been
7 on the market. But the argument that's been made here is that
8 the sequencers are the second solid support; right? The
9 Illumina sequencers that Illumina sold to Ariosa are the second
10 solid support, and do the detection.

11 **Q.** Page 333, line 19 through 334, line 3.

12 **A.** Sorry. Which page?

13 **Q.** 333.

14 **THE WITNESS:** Thank you. You probably have looked at
15 this more recently than I.

16 **MR. HEINRICH:** Excuse me a moment.

17 **MR. REINES:** Of course.

18 **THE WITNESS:** Sure.

19 **MR. REINES:** Everybody got it? Okay.

20 **MR. HEINRICH:** Just one moment, please.

21 **MR. GINDLER:** Hold on.

22 **MR. REINES:** Sure.

23 All right. Play it, please.

24 (Videotape was played but not reported.)

25

1 BY MR. REINES

2 Q. In order to -- you don't need the '794 patent to use the
3 Illumina sequencers; right? You acknowledge that?

4 A. I'm not going to offer an opinion on that, no.

5 Q. Do you know whether you need to use the Golden Gate
6 protocol in order to use the Illumina sequencers; or do you
7 know that there's a lot of other ways you can use them?

8 A. Golden Gate, we haven't talked about, and I'm not willing
9 to offer an opinion on whether one can use the sequencer. I
10 don't know what the licensing agreements are, so I can't offer
11 an opinion on that.

12 Q. Have you ever used an Illumina sequencer?

13 A. Yes, I have.

14 Q. Have you done it without using the Golden Gate approach?

15 A. Golden Gate is a different assay than what's involved in
16 sequencing.

17 Q. Thank you. All right. I'd like to turn to the '430
18 patent, please; and let's turn to Step F, which is Exhibit 514,
19 page 64.

20 (Document displayed.)

21 THE WITNESS: You can be my assistant. Thank you.

22 BY MR. REINES

23 Q. All right. And if we could pull that up.

24 I'd like to highlight "comprising."

25 Do you see that?

1 A. Sure.

2 Q. Now, you've been an expert in enough patent cases that you
3 know what "comprising" means; right?

4 A. I have an understanding of what "comprising" means.

5 Q. And "comprising" means that in order to perform the
6 function that's described above, of determining, to perform
7 that step of determining I should really say, that comprising
8 means you need to perform the using step that follows. But you
9 can do other things, too; correct? You know that?

10 A. I'll assume your legal definition is correct. I'm not
11 going to offer a legal opinion on what exactly "comprising"
12 means.

13 Q. But in terms of your opinions in this case, you have
14 accepted that premise for your opinions; right?

15 A. I understand that "comprising" means you can do other
16 things.

17 Q. Okay.

18 MR. REINES: I think that's it. Thank you.

19 THE COURT: Anything further, Mr. Heinrich?

20 REDIRECT EXAMINATION

21 BY MR. HEINRICH

22 Q. Just a few things here.

23 First, counsel asked you some questions about Claim 2 of
24 the '794 patent.

25 A. Yes.

1 Q. Do you recall now that plaintiffs actually dropped their
2 infringement claim under Claim 2 of the '794 patent?

3 A. Yes, I believe that's correct.

4 Q. Okay. You also --

5 MR. REINES: Your Honor, I don't -- we didn't -- I
6 don't believe we dropped claim.

7 MR. HEINRICH: I don't believe that Dr. Cooper
8 addressed it.

9 MR. WALTER: He did.

10 MR. REINES: He did. I don't know what the answer
11 was.

12 BY MR. HEINRICH

13 Q. So if you don't meet A and B of Claim 1, can there be any
14 infringement of any claim in the '794 patent?

15 A. Not -- all of the other claims require that you do
16 Claim 1. So if we don't do Claim 1, you don't practice the
17 other claims.

18 Q. Now, you were asked some questions about testimony from
19 someone else in a different proceeding.

20 Was that individual testifying about the Harmony™ assay?

21 A. To my knowledge, no. I don't know what he was talking
22 about.

23 Can I find this? I'm not sure what he was talking about,
24 but he was probably -- I have no idea what he was talking
25 about; but I think he was talking about something actually very

1 different - a different kind of assay. He said -- I believe --
2 and I can't find the exact text, but if you read it, it said
3 there could be some advantages to doing solid state
4 hybridization or solid state binding and then hybridization.

5 One of the ways we often use this technology is to purify
6 DNA. So we can take a bead with a probe and attach sequences
7 and pull them out and then do subsequent hybridization. If you
8 do that -- right? -- you've got rid of all of the other mess
9 that can interfere. And that can give you an advantage.

10 So, you know, the fact -- one of the words in there that I
11 think he used actually suggested the purification reducing
12 complexity, I think, leads me to believe he was talking about
13 something else.

14 Q. All right. Now, you were asked some questions about the
15 Version 1 SOP.

16 A. Right.

17 Q. If you could pull up Trial Exhibit 55 and go to Section
18 13.8.

19 Now, does the SOP actually describe somewhere in it the
20 order of steps, the actual procedures in the lab?

21 A. Yes, it does.

22 Q. And is this one of those places in the SOP that actually
23 describes sort of the step-by-step process?

24 A. Yeah, it's not the background section; it's the actual
25 laboratory protocol.

1 Q. And did counsel show you this section in his
2 cross-examination?

3 A. No, he didn't.

4 Q. And what does this section make clear from the SOP?

5 A. So it says:

6 "In the anneal PNA task, a purified cell-free DNA is
7 resuspended and annealed with the DANSR probes."

8 Right? So they're telling us that the cell-free DNA
9 is now annealed with those probes. It's a
10 double-stranded complex.

11 Q. So in terms of the steps, is it your understanding that
12 those steps have to be met literally, that there's no doctrine
13 of equivalents for those steps?

14 A. Right. The steps have to be performed in a particular
15 order.

16 Q. So close enough isn't enough?

17 A. Close enough isn't enough.

18 Q. And is it your understanding that it's Illumina's burden
19 to prove that at least a hundred single-stranded target
20 sequences have to be first bound to a solid support, and then
21 hybridized to a probe, and then go through the process and be
22 detected?

23 MR. REINES: Objection. Leading.

24 THE COURT: Sustained.

25

1 BY MR. HEINRICH

2 Q. So what's your understanding with respect to the burden on
3 those specific issues?

4 A. The --

5 MR. REINES: Objection. Vague.

6 THE COURT: Legal question. What?

7 BY MR. HEINRICH:

8 Q. It -- well, so is probability --

9 Did you set out to try to disprove their arguments on
10 infringement?

11 A. It's hard to disprove that nothing is there, all right?

12 And we have seen no evidence at all that there's
13 single-stranded DNA attached to these beads.

14 Q. Okay. And then one last question.

15 You showed some slides on sort of the background concepts
16 of detecting aneuploidy, slides 45 and 46 --

17 A. Mm-hm.

18 Q. -- showing a basic comparison.

19 Was that in reference to FORTE?

20 A. I mean, FORTE doesn't do that; right?

21 FORTE uses these probability models to estimate the risk
22 of aneuploidy. So those are really to talk about, you know,
23 amniocentesis and give a general background of the idea; but it
24 doesn't describe what FORTE does.

25 Q. And finally, you mentioned Golden Gate. You were asked a

1 question about Golden Gate.

2 So were you using that interchangeably with the patent,
3 the '794 patent?

4 **A.** Absolutely not.

5 My understanding is Golden Gate is a different patent
6 referring to a different invention.

7 **MR. REINES:** Objection, Your Honor.

8 **MR. HEINRICH:** Thank you very much.

9 **MR. REINES:** I would move to strike that. The
10 opinion on Golden Gate Mr. Gindler assured me would not go in
11 front of Dr. Quackenbush.

12 **MR. HEINRICH:** Counsel opened the door.

13 **MR. REINES:** I didn't open the door to anything about
14 whether it read on Claim 1. I had asked about whether it read
15 on Claim 1. I didn't ask anything about that.

16 **THE COURT:** You asked about Golden Gate.

17 **MR. REINES:** Okay.

18 **MR. HEINRICH:** Thank you.

19 **THE COURT:** All right. Anything further?

20 (Discussion off the record.)

21 **THE COURT:** Anything further?

22 **MR. REINES:** Yeah, I have to consider, because I
23 just -- a new opinion came out.

24 **THE COURT:** Oh, okay.

25 (Discussion off the record.)

1 **MR. REINES:** Okay. Yeah, let's do one.

2 **RECROSS-EXAMINATION**

3 **BY MR. REINES:**

4 **Q.** In reading the patent, did you understand Claim 2?

5 **A.** Yes.

6 **Q.** All right. I'd like you to turn to -- well, actually, let
7 me just -- we'll just leave it there.

8 Did you -- let's do this.

9 Figure 13 -- are you familiar with that in the '794 patent
10 as part of your work in this case?

11 **A.** Yes. And it's been shown here, too.

12 **Q.** And you'll acknowledge that Figure 13 is covered by Claims
13 19 and 20; correct?

14 **A.** I'd have to look at Claims 19 and 20.

15 The figures in the patent don't necessarily refer to the
16 claimed invention. And those same figures were used in
17 different patents.

18 **Q.** Okay. You'll acknowledge -- are you aware that Figure 13
19 is stated to be the Golden Gate invention by Dr. Stuelpnagel?

20 **A.** I don't remember what Dr. Stuelpnagel said.

21 **Q.** And you'll agree that Figure 13 is covered by the claims,
22 then it would cover the invention of Dr. Stuelpnagel?

23 **A.** I'd have to look at the claims and really analyze them.
24 And I haven't looked at those claims in a long time.

25 **Q.** Okay. So in this question of inventorship by

1 Dr. Stuelpnagel and Dr. Oliphant, you haven't prepared an
2 opinion in this case on that?

3 **A.** I have no opinion on inventorship.

4 **THE COURT:** Anything further?

5 **MR. HEINRICH:** Nothing further.

6 **THE COURT:** Thank you very much, sir. You may step
7 down.

8 **THE WITNESS:** Thank you.

9 Okay. Defendant may call its next witness.

10 **MS. HABERNY:** Ariosa calls Professor Charles Cantor.
11 (Whereupon a document was tendered to the Court.)

12 **THE CLERK:** So I'm going to take your picture.

13 **MR. REINES:** Your Honor, just a quick request.

14 Can we label the drawing with the Gaussian curve as just
15 for identification in this case?

16 **THE COURT:** Sure.

17 **MR. REINES:** We may want to refer to it.

18 **THE COURT:** In fact, we should probably label all of
19 those things that he --

20 **MR. REINES:** No. No objection.

21 **THE CLERK:** We can do that on the break.

22 Please raise your right hand.

23 **CHARLES CANTOR,**
24 called as a witness for the Defendants, having been duly sworn,
25 testified as follows:

1 **THE WITNESS:** I do.

2 **THE CLERK:** Thank you. Go ahead and state your full
3 name for the record.

4 **THE WITNESS:** My name is Charles Robert Cantor,
5 C-A-N-T-O-R.

6 **THE COURT:** Ms. Haberny.

7 **DIRECT EXAMINATION**

8 **BY MS. HABERNY**

9 **Q.** Good morning, ladies and gentlemen.

10 Good morning, Professor Cantor.

11 **A.** Good morning.

12 **Q.** Professor, have you been present for almost all of the
13 testimony that's been given in this trial?

14 **A.** I've been here except for the first day. I was trapped by
15 a snowstorm in New York.

16 **Q.** Thank you. And what are you here to testify about today?

17 **A.** I am here to testify about the invalidity of the '794
18 patent, and the '430 patent.

19 **MS. HABERNY:** Your Honor, may I approach to move the
20 professor's microphone?

21 **THE COURT:** Sure.

22 **MS. HABERNY:** It will be easier.

23 **THE WITNESS:** I'm struggling to have both the chair
24 and the microphone.

25 **THE CLERK:** I think you can angle it so you're more

1 comfortable. Let's adjust it. (Indicating)

2 **THE WITNESS:** Thank you.

3 **BY MS. HABERNY:**

4 **Q.** Professor, what are your opinions about the invalidity of
5 the '794 patent?

6 **A.** I think the '794 patent is not valid. I think that it's
7 anticipated by prior art.

8 **Q.** And what prior art would that be?

9 **A.** Straus patent -- sorry. Straus patent application, yeah.

10 **Q.** By inventor Straus?

11 **A.** By inventor Straus.

12 **Q.** And what are your opinions about the invalidity of the
13 '430 patent?

14 **A.** I think the '430 patent is not valid, because it -- the
15 inventors didn't really possess the full scope of the claims,
16 and they don't teach you -- they don't teach a person of the
17 state of the art how to practice those claims without undue
18 effort.

19 **Q.** And I'd like to first ask you some questions about your
20 background.

21 Would you please tell the jury about your educational
22 history?

23 **A.** Sure. I was an undergraduate at Columbia in
24 New York City, and then a graduate at the University of
25 California Berkeley.

1 Q. And how long have you been a professor?

2 A. About 45 years.

3 Q. And where have you taught?

4 A. I've taught at Columbia, I've taught at U.C. Berkeley, and
5 I've taught at Boston University.

6 Q. And how many publications have you made?

7 A. Well, I stopped counting after 450.

8 Q. And have you published any textbooks?

9 A. Yeah, I published a three-volume textbook in biophysical
10 chemistry and I published a textbook in genomics. So both of
11 those are quite relevant to the topic matter here.

12 Q. And how many scientists have you trained in your
13 laboratory?

14 A. Again, I stopped counting, but at least 50 graduate
15 students and 50 post-docs.

16 Q. And do any of the graduate students you've trained have a
17 connection to this case?

18 A. Yes, they do. And Dr. Fan, one of the inventors of the
19 '794 patent, was my doctoral student at Columbia.

20 Q. Is that the same Dr. Fan that was shown during Professor
21 Quackenbush's presentation?

22 A. Exactly the same.

23 Q. What did Doctor Dr. Fan study in your lab?

24 A. He studied the structure of the genome of yeast
25 microorganism.

1 Q. Did you personally train Dr. Fan?

2 A. I personally supervised him, and it was a pleasure.

3 Q. Are you an inventor on any patents?

4 A. I have a lot of patents. Again, I stopped counting, but I
5 have at least 65 U.S. patents.

6 Q. Are you member of any special scientific academies or
7 organizations?

8 A. Yeah, among others, I'm a member of the U.S. National
9 Academy of Sciences, and I'm a member of the new U.S. National
10 Academy of Inventors.

11 Q. And the jurors have now heard a lot about the Human Genome
12 Project in this case.

13 Did you have any involvement in the Human Genome Project?

14 A. Yes, I did. I was one of the people that started it, and
15 I ran the Department of Energy's portion of it for several
16 years when I was at Berkeley.

17 Q. And could you give the ladies and gentlemen of the jury a
18 bit more flavor.

19 Would you briefly describe what the effort of the Human
20 Genome Project was?

21 A. So that project determined the full DNA text of one human
22 individual, about 3 billion base pairs, but it also developed
23 all the methodology to do this, because that was
24 groundbreaking.

25 Q. And the jury's also heard a lot about a company called

1 Sequenom in this case.

2 Do you have any history with Sequenom?

3 **A.** Yeah, I was one of the three people that founded Sequenom
4 in 1994, and I was its Chief Scientific Officer from 1998 to
5 2013.

6 **Q.** And would you please remind the jury why Sequenom is
7 relevant to this case?

8 **A.** Yeah. So Sequenom -- in the 21st Century -- developed
9 non-invasive prenatal testing. It became the first commercial
10 purveyor of non-invasive prenatal testing. Today is still the
11 market leader, but it's now owned by LabCorp.

12 **Q.** Would you please tell the jury whether you relied on all
13 of this experience in forming the opinions that you're going to
14 give here today?

15 **A.** Yeah. I was working in this exact field, both in the time
16 frame of the '794 patent, which is about the year 2000, and in
17 the time frame of the '430 patent, which is the year 2010.

18 **Q.** And aside from that, what materials did you consider in
19 reaching your opinions today?

20 **A.** Well, of course I read the patents. I read some of the
21 references that are cited in the patents. I read some other
22 prior-art references. I read the depositions of various
23 declarations of some of the other experts and participants; and
24 I read corporate reports from I think both Illumina and Ariosa.

25 **MS. HABERNY:** Your Honor, I would like to offer

1 Professor Charles Cantor as an expert on the invalidity of the
2 '794 and '430 patent.

3 **MR. REINES:** Your Honor, no objection. No *voir dire*
4 now, but I reserve the right to ask some questions about his
5 qualifications, and so forth, during the course of his --

6 **THE COURT:** Very well. You may proceed.

7 **BY MS. HABERNY:**

8 **Q.** Professor Cantor, you referred to the Straus patent
9 application as the reference that anticipates the '794, patent
10 claims?

11 Would you please turn to Exhibit 1044 in your binder?

12 Is this the Straus reference you were referring to?

13 **A.** Yes, it is.

14 **MS. HABERNY:** Your Honor, I move to admit
15 Exhibit 1044 into evidence.

16 **MR. REINES:** No objection.

17 **THE COURT:** It will be received.

18 (Trial Exhibit 1044 received in evidence.)

19 (Document displayed.)

20 **BY MS. HABERNY**

21 **Q.** And before we get into the substance, would you please
22 tell the jury what anticipation standard you applied in
23 reaching your opinion that the '794 patent is anticipated by
24 the Straus reference?

25 **A.** Yeah. So to anticipate a patent, prior art has to

1 describe every aspect of the claims in that patent. In other
2 words, it has to essentially be the almost an identical prior
3 invention.

4 Q. And in lay terms, is it your understanding that if the
5 '794 patent is anticipated, then that simply means that someone
6 else invented it first?

7 A. Yes, exactly.

8 Q. Was the Straus patent application reference filed before
9 the earliest priority date of the '794 patent?

10 A. It was filed 14 months earlier.

11 Q. And what's the general subject area of the '794 patent?

12 A. The '794 patent describes methods for looking at a sample
13 and analyzing many different DNA sequences in that sample,
14 simultaneously. It's something that we call multiplex
15 detection of multiplex analysis.

16 Q. And what's the general subject matter of the Straus
17 reference?

18 A. Exactly the same.

19 Q. So before we dive into the meat of Straus, what's your
20 overall impression.

21 THE COURT REPORTER: I'm sorry. Before you dive into
22 what of Straus?

23 BY MS. HABERNY:

24 Q. Into the meat, into the substance of the Straus reference.

25 What is you're overall impression of this reference?

1 A. Well, in my opinion I've never seen such a beautiful piece
2 of prior art, because almost everything that we need to talk
3 about is contained within a single figure.

4 Q. And which figure would that be?

5 A. Figure 5.

6 Q. Thank you. Would you first please show the jury
7 physically what exhibit this is, what it looks like?

8 A. So this is a patent. (indicating). And the figure is
9 about eight pages in.

10 Q. Thank you.

11 A. I want to show you a gigantic version of this figure in a
12 moment, so we can work better.

13 Q. As Professor Cantor just mentioned, we have a blown up
14 version of Figure 5 on a board here.

15 MS. GLASSER: Dr. Cantor?

16 THE WITNESS: You know what, it's very tall.

17 MS. GLASSER: It is very tall.

18 THE WITNESS: Do I take the microphone with me?

19 MS. HABERNY: No, you don't need it.

20 MS. GLASSER: Do you want it down there instead?

21 THE WITNESS: Not the same. I won't be able to see
22 it.

23 THE COURT: Tracy, do we have a pointer?

24 THE CLERK: What number is that exhibit?

25 MS. HABERNY: 1044.

1 **MR. REINES:** Your Honor, I'd just ask that we stay in
2 question and answer.

3 **THE COURT:** Yeah, we can, but I --

4 **THE CLERK:** I don't -- I might have a pointer, but my
5 closet is broken, and I can't --

6 **MS. HABERNY:** It's okay. We don't need one.

7 **THE COURT:** Okay. But do Q and A.

8 **BY MS. HABERNY:**

9 **Q.** Would you please give a brief overview of what Figure 5 is
10 showing?

11 **A.** Yeah. So Figure 5 is showing -- there's a flowchart of a
12 process in which we are starting with a sample and analyzing
13 many DNA fragments simultaneously. So we're putting the sample
14 on a solid surface. We're adding DNA probes. Those probes are
15 hybridizing to what's on the surface. We're then adding an
16 enzyme, and it's ligating those probes together, if they're --
17 if they have complementary sequences to the sequences on the
18 surface. We're then washing. We're amplifying those probes to
19 make many copies. We are then attaching these amplicons to a
20 second solid surface, which happens to be an array; and we're
21 then detecting which particular targets in the sample are now
22 present on the array.

23 **Q.** Thank you. And I'd like to now start mapping the '794
24 patent claim elements to this figure.

25 So let's start with the preamble, if could call that up.

1 So the preamble of the '794 patent, Exhibit 513, reads:
2 "A multiplex method for determining whether a sample
3 contains at least 100 different target sequences."

4 Do you see that in Straus Figure 5?

5 **A.** Yeah. So this is the preamble: "Scanning a clinical
6 sample for numerous pathogens" - pathogens are just DNA
7 sequences in a sample.

8 **Q.** Where does Straus disclose the at least 100 different
9 target sequences?

10 **A.** So that's not mentioned in the figure; it just says
11 "numerous;" but in the body of the patent, it talks
12 specifically about a hundred target sequences.

13 **MS. HABERNY:** And Mr. Simmons, would you please pull
14 up paragraph 138 of the Straus reference, which is
15 Exhibit 1044?

16 (Document displayed.)

17 **THE WITNESS:** So ID sequences are target sequences.

18 **BY MS. HABERNY:**

19 **Q.** And this is your reference to at least 100 of them?

20 **A.** Yes.

21 **Q.** Now, if you can please go back to Exhibit 513, the '794
22 patent, Claim Element 1A.

23 And Professor Cantor, Claim Element 1A recites:

24 "Providing a sample which may contain at least 100
25 different single-stranded target sequences attached

1 to a first solid support."

2 Where do you see that in Figure 5.

3 **A.** So here's our first solid support (indicating). Here's
4 the sample that's been provided (indicating).

5 **Q.** And where do you see that it's single-stranded?

6 **A.** So it says, "denatured." That's a technical term for
7 changing double-stranded DNA into single-stranded DNA.

8 **Q.** And where do you see that the target sequences are
9 attached to the solid support?

10 **A.** It uses the word "fixed;" and fixed just means attached.

11 **Q.** And how do you know that that's a solid support that the
12 single-stranded target sequences are being attached to?

13 **A.** Well, the body of the patent describes it as, for example,
14 a nylon membrane, which is a solid support.

15 **Q.** And that's not a bead, but is it still a solid support?

16 **A.** Well, a membrane is like this piece of paper. It's solid.

17 **Q.** So it doesn't have to be a bead?

18 **A.** No, of course not.

19 **Q.** Let's move to patent Claim Element 1B of the '794 patent;
20 and it says:

21 "Contacting said target sequences with a probe set
22 comprising more than 100 different single-stranded
23 probes."

24 Where do you see that in Figure 5 of Straus?

25 **A.** So here's the probe set. We're just showing two different

1 probes, but they're not going to draw all hundred. And the
2 contacting is hybridization. And you can see that these are
3 different because, for example, of the two, there's a white one
4 and a black one. So illustrating different probes.

5 **Q.** And where does Straus describe more than 100 different
6 probes?

7 **A.** Again, the more than 100 different probes -- I think he
8 actually talks about 250, more than 250 different probes -- is
9 in the body of the patent, not in the figure.

10 **MS. HABERNY:** And Mr. Simmons, can we please pull up
11 paragraph 39 of the Straus Exhibit 1044.

12 **Q.** Would you please tell the jury whether this is the portion
13 of Straus that you're referring to?

14 **A.** Yes, it is.

15 **Q.** Now, can we please go back to the '794 patent and look at
16 Step 1B, little i?

17 And this recites that each of the probes has an identical
18 universal priming site.

19 Professor, do you see that in Figure 5 of the Straus?

20 **A.** Yeah. You could see that this part is the same in the two
21 different types of probes; and you see that they bent it out,
22 as you've seen in other pictures before, to indicate that it's
23 not complementary; it doesn't correspond to anything in the
24 target. It's a universal sequence, a synthetic sequence that's
25 added.

1 Q. And where does Straus disclose that the probes all have
2 identical universal priming sites?

3 A. Again, that's described in the body of the patent, not
4 specifically in the figure.

5 MS. HABERNY: Mr. Simmons, would you please pull up
6 paragraph 176 of the Straus reference, Exhibit 1044.
7 (Document displayed.)

8 BY MS. HABERNY

9 Q. Professor, is this the portion of the specification that
10 you're referring to?

11 A. Yeah. So Straus uses the term "amplification sequence,"
12 instead of priming. Just different word; same thing.

13 And you see this can include one or more, but it could
14 include one only amplification sequence, one primer, universal
15 primer.

16 Q. Thank you. Now let's go back to the '794 patent,
17 Exhibit 513, Claim Element 1B, little i, little i.

18 MS. HABERNY: Mr. Simmons, would you please pull that
19 up?

20 Q. This requires first a target-specific domain.

21 Professor, do you see that?

22 A. Yeah. So this is the target-specific domain.

23 Q. And the claim element also requires a double-stranded
24 hybridization complexes are formed comprising the probes and
25 target sequences.

1 Do you see that in Figure 5?

2 A. Yeah, so here are double-stranded complexes.

3 Q. And Claim Element 1C requires removing unhybridized
4 probes.

5 Is that also shown in Figure 5 of Straus?

6 A. Absolutely. That's a washing step. Wash away probe means
7 removing.

8 Q. And Step 1D of the '794 patent recites:

9 "Contacting said probes of the hybridization
10 complexes with a first enzyme and forming different
11 modified probes."

12 Do you see that in Straus Figure 5?

13 A. I do. So our first enzyme is a ligase. Ligase means to
14 use the enzyme ligase. And the ligase is modifying these
15 probes by linking two adjacent probes together.

16 Q. And would you now, Professor, please look at Claim
17 Element E.

18 If we could pull that up on the screen.

19 (Document displayed.)

20 **BY MS. HABERNY**

21 Q. In lay terms for the jury, what is '794 patent Claim
22 Element 1E describing?

23 A. This is just an amplification step. You've heard about
24 amplification. We're going to make many copies starting from
25 one copy.

1 Q. And do you see that amplification step of 1E in Straus
2 Figure 5?

3 A. Amplify. (indicating).

4 Q. And moving on to '794, Claim Element 1F, this recites:
5 "Immobilizing said different amplicons to a second
6 solid support."

7 Where do you see that in Straus Figure 5?

8 A. So here's the second solid support (indicating), and it
9 says the probes after amplification are being hybridized to
10 that support.

11 Hybridization is being used to immobilize to the second
12 solid support.

13 Q. Finally, where do you see the first part of Claim
14 Element 1G, which recites:

15 "Detecting said different amplicons immobilized to
16 said second solid support."

17 A. Yeah. So this particular patent uses detection sequences
18 to direct the amplified products to particular spots on the
19 array; and so that's the detection we ask: "Where did it go on
20 that array?"

21 Q. And finally, the final part of Claim Element 1G recites:
22 "Determining whether the sample contains at least 100
23 different target sequences."

24 Where do you see that?

25 A. Yeah. So each detection sequence corresponds to one

1 target sequence. And there are lots and lots of detection
2 sequences here.

3 **Q.** And is that basically the same thing that the preamble
4 said?

5 **A.** Yes.

6 **Q.** Thank you. So in sum, would you please tell the jury
7 whether it's your opinion that the Straus Figure 5, with those
8 additional disclosures from the body of the specification,
9 anticipates every element of Claim 1?

10 **A.** Yeah, it's virtually identical. They just occasionally
11 use different words, but the concepts, the procedures are the
12 same.

13 **Q.** Now let's move on to patent Claims 2 and 13 of the '794
14 patent. These both require substantial complementarity at
15 detection and interrogation positions for the enzyme to modify
16 the probes.

17 Is that described in Straus?

18 **A.** Yes, it is. So I need to just remind the jury that
19 substantial complementarity is a technical term that is
20 specifically defined in this patent. And what it means is
21 sufficiently similar to hybridizing. So anything that can
22 hybridize is substantially complementary. And if I cannot
23 hybridize, it is not substantially complementary.

24 So you can see here, non-specifically bound probe heads,
25 that is those that are not substantially complementary to the

1 target, cannot be acted upon by the enzymes. So that's exactly
2 what claims, I guess, 2 and 13, is that --

3 Q. 2 and 13.

4 A. Right. Yeah. Yeah.

5 Q. Would you please tell the jury whether it's your opinion
6 that Straus Figure 5 anticipates the additional elements of
7 Claims 2 and 13?

8 A. Yes, it does.

9 Q. And '794 patent Claim 3 recites that the second solid
10 support is an array.

11 Can you show the jury where that is in Figure 5?

12 A. Here's or detection array. That's the second solid
13 support.

14 Q. And is it your opinion that Straus Figure 5 anticipates
15 Claim 3?

16 A. Yes, it does.

17 Q. And would you please tell the jury -- oh, can we pull up
18 Claim 9, please?

19 (Document displayed.)

20 **BY MS. HABERNY**

21 Q. So '794 patent Claim 9 recites that the probes are ligated
22 to other probes.

23 Do you see that in Straus Figure 5?

24 A. Yes, I do. So I've already explained the particular
25 enzyme that Straus used was ligase.

1 So here is our Claim 9.

2 **Q.** And is it your opinion that Claim 9 is anticipated by
3 Straus?

4 **A.** Most definitely.

5 **Q.** So in your opinion, Professor Cantor, are all of the
6 asserted claims of the '794 patent invalid over Straus?

7 **A.** That's my opinion, yes.

8 **Q.** Thank you.

9 You can sit down. And I'll move the board.

10 **MS. GLASSER:** I can do it, Sandy. It's okay.

11 **THE WITNESS:** It's too big for me.

12 **BY MS. HABERNY:**

13 **Q.** Now I'd like to turn to the '430 patent.

14 What are your opinions on the invalidity of the '430
15 patent claims?

16 **A.** So I think the '430 patent is invalid because the
17 inventors didn't possess the full scope of the claims. That
18 is, they couldn't have actually practiced this patent from
19 what's described in the patent; and certainly it doesn't --
20 it's not enabled. In other words, it doesn't contain enough
21 substance to teach somebody else who was an expert in the
22 field. Sorry. A person, not an expert, a person in the state
23 of the art in the field. It doesn't contain enough information
24 to teach such a person how to practice the full scope of the
25 claims without an enormous amount of effort.

1 Q. And are those concepts that you just described referred to
2 in legalese as written description and enablement?

3 A. Thank you. I'm trying to stay away from the legalese;
4 right.

5 Q. And as of what date are you viewing what the person of
6 skill in the art that you just mentioned would have understood
7 from the patent?

8 A. Well, the reference period for the '430 patent is about
9 2010.

10 Q. And why is that?

11 A. Because that's when the patent was filed.

12 Q. Okay. Is it your opinion that the '430 patent lacks
13 written description and enablement based in part on your own
14 experience?

15 A. Yes. Actually, so we haven't described the patent yet, so
16 perhaps I need to say something about what this patent is.

17 Q. Well, sure, just --

18 A. Yeah. But based on my own experience, I think this patent
19 would work.

20 Q. And what experience would that be?

21 A. Well, at Sequenom, we've been trying to do almost the same
22 thing, and we failed miserably. It's a very hard task.

23 MS. HABERNY: Thank you.

24 Mr. Simmons, would you please pull up the '430 patent,
25 which is Exhibit 514, Claim 1?

1 Q. Professor, would you please explain what Claim 1 is
2 claiming, just a general overview?

3 A. Yeah. I'm not going to read you this claim, because that
4 would use up the rest of my testimony time. But let me just
5 paraphrase the important parts of it.

6 The idea, instead of looking through the whole genome
7 to -- and counting reads of chromosomes to try to look at the
8 relative abundance of difference chromosomes, that you choose a
9 small set of sequences to represent the chromosomes that you're
10 interested in.

11 And you -- it's not such a small set; however, it's at
12 least a hundred different sequences. And you have to
13 simultaneously, after choosing them, select them, that is,
14 physically isolate them or amplify them; and then you have to
15 decide whether or not there's an aneuploidy based on the
16 different number of reads from those particular sequences in a
17 reference chromosome and in the chromosome your testing.

18 So if you're testing for Down Syndrome, it would be
19 Chromosome 21 comparing, let's say, as you saw on the previous
20 testimony, Chromosome 22.

21 Q. Are there particular claim elements that you believe are
22 not described or enabled, or is it a combination?

23 A. It's a combination of elements. But I think the two that
24 trouble me the most -- doing this by memory to save time -- I
25 think there are B and F; but we'll probably see them in a

1 moment; right?

2 **Q.** Can we pull up Claim Element 1F, please?

3 (Document displayed.)

4 **BY MS. HABERNY**

5 **Q.** And what does Claim Element F describe in lay terms for
6 the jury?

7 **A.** So Claim Element F purports to show a method for analyzing
8 the data. So instead of looking at the whole genome, we've
9 looked at just a few hundred sequences chosen from, let's say,
10 from Chromosome 21 versus Chromosome 22. And we're going to
11 try to see if there's an aneuploid based on how many of those
12 model kits, how many of those specific sequences we detected,
13 okay? And this is really the problem.

14 And the problem is that, I think as you saw in the
15 previous testimony, we're looking for a very tiny effect,
16 because the fetal DNA in the mother's blood is diluted by huge
17 amounts of maternal DNA, okay?

18 **THE COURT REPORTER:** I'm sorry. Huge amounts of
19 what, sir?

20 **THE WITNESS:** Oh, huge amounts of maternal, mother's
21 DNA.

22 Okay. So if I -- if I could choose every single fragment
23 I can get from Chromosome 21, that would be 50,000 fragments.

24 If I'm only choosing a hundred, I'm only sampling a small
25 percentage of the chromosome, which means I'm throwing away

1 most of my data, and the measurements are already noisy. And
2 if I throw away most of my data, I'm just making the noise
3 worse and worse, okay?

4 So it's very challenging. And it's why we weren't able to
5 get this to work, at Sequenom, when we tried it with something
6 like 70 or a hundred molecules in this timeframe.

7 **Q.** And would one need a very sophisticated mathematical
8 approach to compensate for this noise that you were just
9 describing?

10 **A.** Yeah. So you heard about the FORTE approach that was
11 developed by Ariosa scientists in previous testimony.

12 Frankly, I don't fully understand it, how that works.
13 Although I have some inkling.

14 But the point is that because you made the data much worse
15 by only using a small portion of it, you have to compensate for
16 this in elaborate ways. And that's what I believe Ariosa
17 invested a huge effort in, and it's why they succeeded where we
18 failed.

19 **Q.** And does the '430 patent teach anything about a
20 mathematical algorithm that could be used to address the
21 problem?

22 **A.** So what the '430 does is incorporates by reference four
23 patents or scientific articles that describe how whole genome
24 sequencing or random shotgun sequencing could be analyzed to
25 detect whether there's an aneuploidy, okay?

1 But as I've just told you, we've made things much worse by
2 not using the whole genome. And that -- you can't use the
3 whole genome analytical methods, they definitely won't work.
4 You'd have to improve on them, and that's what's missing in the
5 patent.

6 Q. You testified that at Sequenom you had tried an approach
7 like this. If you had had this '430 patent in hand when you
8 were trying that method at Sequenom, would that have provided
9 any guidance or teaching?

10 A. It wouldn't have helped me in the slightest. In fact,
11 what we were trying to do around the same timeframe was already
12 more sophisticated.

13 Q. And is it a surprise to you, based on your experience and
14 expertise, that Verinata never commercialized a product that
15 uses the method of the '430 patent?

16 A. No, it doesn't surprise me that they never commercialized,
17 because if they had tried to, it wouldn't have worked.

18 MS. HABERNY: Thank you. Pass the witness.

19 MR. REINES: Thank you.

20 CROSS-EXAMINATION

21 BY MR. REINES

22 Q. Good morning.

23 A. Good morning.

24 Q. How long were you working directly in the NIPT field at
25 Sequenom?

1 A. Well, so -- so you said at Sequenom.

2 I started working in the NIPT field independently of
3 Sequenom, because I was a collaborator with Dennis Lo.

4 Dennis Lo is the pioneer in this field. He's the one who
5 discovered fetal DNA in the mother's blood. And Dennis and I
6 started collaborating in 2001; but that was an academic
7 collaboration. Although I was the Chief Scientific Officer of
8 Sequenom, I still had an academic laboratory in
9 Boston University. And one of my graduate students together
10 with some of Dennis Lo's people, had a very productive -- about
11 five-year -- collaboration.

12 Q. Yeah. When did you leave the NIPT field?

13 A. Oh, I'm sorry. When did I leave the -- I'm still working
14 in the NIPT field.

15 Q. So you're up to date?

16 A. Well, I can't say I'm up to date, because I'm supposed to
17 be retired, and I don't have a library and things like that.
18 But I still have one NIPT project ongoing that I'm very excited
19 about.

20 Q. Okay. The '430 patents about targeted sequencing?

21 A. Yes.

22 Q. And you understand Ariosa's product is about targeted
23 sequencing?

24 A. Yes.

25 Q. And that's different than random sequencing; is that

1 correct?

2 **A.** Yes.

3 **Q.** Okay. As far as you are concerned, based on your
4 knowledge of the field of prenatal diagnostics for years,
5 targeted sequencing is honestly hell; isn't that what your view
6 is?

7 **A.** So, okay, obviously Ariosa got it to work.

8 So -- so it's not completely hell.

9 The reason why we abandoned it at Sequenom at the time was
10 because we weren't -- we couldn't guarantee that we could make
11 it work in a sufficient time period.

12 And the reason has to do with which sequences you choose
13 to target.

14 (Whereupon a document was tendered to the Court.)

15 **THE WITNESS:** Okay. There are a huge number of
16 possibilities, and so it's a very large task.

17 Now, I must confess I'm working on targeted sequencing
18 myself now as an alternative method, but a very different
19 approach.

20 **BY MR. REINES:**

21 **Q.** July 24th, 201 deposition at 238:14 through 239:5.

22 **THE COURT:** 238:14.

23 **MR. REINES:** 14.

24 **MS. HABERNY:** Can you give me a moment, please?

25 **MR. GINDLER:** Mr. Reines, July 24th?

1 **MR. REINES:** July 24th, yes.

2 **BY MR. REINES**

3 **Q.** All right. Everyone got it? Time is of the essence for
4 everybody.

5 (Videotape was played but not reported.)

6 **Q.** That was your testimony in 2017; right?

7 **A.** That's correct.

8 **Q.** And you knew Ariosa's product was on the market for five
9 years at that time?

10 **A.** I probably hadn't thought about it; but, yes, I must have
11 known that, yeah.

12 **Q.** Okay. And let me ask you another question about that same
13 topic.

14 You also viewed targeted sequencing in 2017 -- you viewed
15 targeted sequencing as more expensive than random sequencing;
16 correct?

17 **A.** So the -- you have to factor in the cost of the targeting.
18 And -- and let me try to say it simpler.

19 Sequencing costs are dropping by a factor of 10 every
20 year, okay? Already by 2017 -- sorry -- by 2013, when I left
21 Sequenom, the cost of getting the sample was more than the cost
22 of the sequencing, okay? So any steps you add, that cost
23 money, and targeting costs money; and however you do it is
24 actually making the test more expensive.

25 That wasn't true when sequencing was very expensive; but

1 it's almost inconceivable to realize how things change by a
2 factor of 10 every year.

3 I'm in a completely different world than I was six years
4 ago.

5 **Q.** But this was true in 2010 to 2012 when Ariosa made a
6 decision to go into targeted sequencing; wasn't it true at that
7 point in time?

8 **A.** I'm sorry. What's the antecedent to this?

9 **Q.** That targeted sequencing was more expensive than the
10 approach that was adopted by Verinata.

11 **A.** No, no, I think -- okay. I wasn't inside Ariosa. I
12 wasn't party to their decision making; but I heard Dr. Song's
13 testimony a few days ago, and I realized then -- I actually
14 hadn't realized before -- how important it was to Ariosa to
15 make an inexpensive test.

16 **Q.** Okay.

17 **A.** And if you're going to make an inexpensive test that
18 you're willing to preselect the most common defects, the most
19 common aneuploidies, and limit the test to those; and that
20 makes the problem much simpler. So that's what they did.

21 **Q.** 239, line 6 through 240, line 6.

22 **A.** Yes.

23 **MR. REINES:** I have to wait for counsel to review it,
24 in fairness.

25 **MS. HABERNY:** Oh.

1 **MR. REINES:** Okay. Let's play it.

2 (Videotape was played but not reported.)

3 **A.** I said across the U.S.

4 **Q.** That was your testimony in 2017; is that correct?

5 **A.** That was my testimony.

6 **Q.** Okay. Let's talk about the '430 patent and your opinion
7 regarding whether Dr. Rava and Dr. Chuu adequately disclosed
8 their invention in there.

9 And you're saying they didn't; is that correct? That's
10 your opinion?

11 **A.** That's correct.

12 **Q.** Okay. Were you here when Dr. Rava testified?

13 **A.** I was.

14 **Q.** Okay. With respect to what a person of ordinary skill in
15 the art would know, looking at the disclosure of the '430
16 patent, they would be assumed to have the knowledge of all of
17 the prior art; right?

18 **A.** Yes.

19 **Q.** Okay. And some of the prior art that you're aware of is
20 the Quake reference and the Craig reference; right?

21 **A.** There are many, many Quake references, so I'm not sure
22 which one you're talking about.

23 Could you -- could you sort of define for me the
24 technology that the reference pertains to?

25 **Q.** Sure. You relied on the Quake and Craig references to say

1 that the claim requirement of 100 sequences -- there's this
2 concept of enriching sequences -- that using the prior art you
3 could do it to 10,000 non-random sequences; right? That's one
4 of your opinions?

5 **A.** Yeah, so this is out of context. I'm still not even sure
6 exactly which reference we're talking about.

7 **Q.** Okay.

8 **A.** If you'd turn to your report at 194, paragraph 387.

9 **MS. HABERNY:** Mr. Reines, would you give me a moment,
10 please, to find this?

11 **MR. REINES:** Of course.

12 **THE WITNESS:** Sorry. Would you give me the numbers
13 again, please?

14 **MR. REINES:** Yes, at 194, paragraph 387.

15 **THE WITNESS:** 387, yeah.

16 **BY MR. REINES:**

17 **Q.** Right. And there you're saying that the claim
18 requirements that you're saying aren't properly disclosed in
19 the '430 patent were actually disclosed by Quake and Craig;
20 correct? That's what the opinion is that you have in your
21 report?

22 **A.** Well, so I'm not -- I'm still having difficulty following
23 you, but let me try to clarify.

24 The reference you drew my attention to just now, that
25 particular Quake reference has nothing to do with sequencing;

1 it's a technology probe digital PCR.

2 **Q.** I'm just asking you in terms of what your opinion was
3 that's set forth in your report, the claim requirements -- feel
4 free to look at what you need to look at -- that you said
5 aren't adequately disclosed in the '430 patent, you have an
6 opinion that when you use Quake plus Craig, they're actually
7 disclosed; right?

8 **A.** I think --

9 **Q.** At one point you were arguing that; right? Isn't that
10 true?

11 **A.** So I -- I haven't looked at this in a long time, and I
12 don't -- I'm having a hard time following what you're asking.

13 Maybe you can ask it a different way.

14 **Q.** Sure. Do you recall arguing that Quake and Craig
15 disclosed certain elements of the '430 patent.

16 Do you remember that?

17 **A.** Yeah, I think what you're talking about is, we were --
18 this was a -- a prior art argument, which we're not making
19 anymore.

20 **Q.** You've abandoned that; right?

21 **A.** Yes. Yeah.

22 **Q.** Okay. But at one point you put in your report that you
23 served on us the information that we had to go by; and then you
24 said that you thought Quake and Craig disclosed the exact same
25 elements that you're saying a person of skill in the art

1 wouldn't know; isn't that true?

2 **A.** So I need to clarify. Now I understand what you're
3 asking, so I need to clarify here.

4 **Q.** Okay. Thank you.

5 **A.** So that Quake reference attempted to do prenatal
6 diagnostics using a single target sequence and a single
7 reference sequence. Not hundreds, but one, okay? And it
8 worked if the mother had a lot of fetal DNA. I believe it
9 worked, so long as the mother had at least 10 percent fetal
10 DNA; but it absolutely failed if the mother had less than
11 10 percent DNA.

12 And that's the whole name of the game in prenatal
13 diagnostics, is trying to devise an assay which is sufficiently
14 inclusive so you cover most pregnant women.

15 And the way in which the '430 patent attempted to do that
16 was to add builds as this prior art -- prior art argument
17 indicates. It builds on the prior digital PCR work, which was
18 the ultimate in focused attention, because we first want
19 target. It attempts to add more and more targets to gain
20 enough sensitivity, to gain enough signal to cover those
21 mothers that have small amounts of fetal DNA.

22 And the problem is that the '430 patent doesn't teach you
23 the requirements -- the good targets, and bad targets.

24 **Q.** Okay. I didn't want to interrupt, but I think we haven't
25 responded for long enough.

1 Let me ask you just really to concentrate on my question,
2 okay?

3 In terms of the claim requirements that you're now
4 contending aren't adequately disclosed in the '430 patent, your
5 opinion in your very expert report that you provided was that
6 the prior art Quake and Craig references adequately disclose
7 that to a person of skill in the art; isn't that true?

8 **A.** That's what I said.

9 **Q.** Okay. That's the question to you.

10 All right. All right. And let me ask you -- and just the
11 person that's approaching the '430 patent is presumed to have
12 complete knowledge of the Quake and Craig references; correct?

13 **A.** Well, the Quake is included by reference. I don't
14 remember whether the Craig is.

15 **Q.** Okay. But you don't deny that Craig is another reference
16 that you said that disclosed --

17 **A.** No, I don't --

18 **Q.** Let me finish.

19 **A.** Yeah. Sorry.

20 **Q.** You don't deny that Craig is another prior art reference
21 that a person of skill in the art would have access to that
22 sufficiently discloses the claim requirements that you're now
23 challenging; right?

24 **A.** Craig teaches indexing, which we haven't discussed at all;
25 but, yes.

1 Q. Okay. The answer is yes? Okay.

2 And now you make an argument that you don't think Dr. Rava
3 adequately described what his invention was?

4 A. That's correct.

5 Q. And you don't think the claims describe that?

6 A. I -- I think that you would not be able to actually carry
7 out what's instructed in the '430 patent without adding a huge
8 amount of extra effort to discover hundreds or thousands of
9 sequences, which not only behaved well and were the same in all
10 people -- because you can't use sequences that are different in
11 different people -- but how do you get them to work all at once
12 together in 2010? This was a very big challenge.

13 Q. So the essence of your argument regarding the '430 patent
14 on an overall basis is that a person of ordinary skill in the
15 art would not be able to make it work; is that correct?

16 A. That's correct.

17 Q. Okay. As to whether Dr. Rava had possession of the
18 inventions that he claimed in it -- that's a different issue
19 that you're not contending; right?

20 A. Ah, so I am actually concerned that he didn't have
21 possession.

22 Q. Do you really know?

23 A. Of course I don't really know. I wasn't there; right?

24 Q. Okay. And based on the documents you reviewed, including
25 the patent, you don't really know; right?

1 A. Well, well, I -- the reason why I'm questioning his
2 possession of the invention is that this is unfortunately
3 pretty sophisticated, the notion of choosing a hotspot to work
4 with in NIPT, to me, actually teaches against the best -- away
5 from what would be the best strategy to focus on.

6 Q. But, Professor, again, that's just -- you're just
7 questioning it. You don't really know; right?

8 A. I wasn't there, yeah.

9 Q. And you don't really know; right?

10 A. I wasn't there, yeah. I don't know.

11 Q. And you don't know; right?

12 A. Yeah, right.

13 Q. Okay. Now, with respect to the numbered sequences, one of
14 the things that you put in your report that you thought Quake
15 disclosed was up to 10,000?

16 A. No. I'm sorry. We're confusing two different things.

17 In digital PCR, you have one or two sequences, and you're
18 sampling individual molecules.

19 So the paragraph 387, which you directed my attention to,
20 is talking about between 500 and a hundred thousand samples.
21 By that they mean individual amplifications.

22 So you do -- you amplify individual molecules and
23 individual little wells; and they're using a hundred thousand
24 different wells in principle, yeah.

25 Q. All right. Let's move to the '794 patent.

1 And that's -- that really covers a multiplexing nucleic
2 acid reactions; you understand that?

3 A. That's correct, yeah.

4 Q. And you said that at the time that you were in the field,
5 you were very familiar with this space; is that correct?

6 A. This is now 2000?

7 Q. Yeah, around then, yes.

8 A. Ten years earlier; right.

9 Q. Right. And you were aware of the Golden Gate product when
10 it came out? Is that something in your field?

11 A. We never used it. And I, frankly, I never paid much
12 attention to it. It was a competitor of some of Sequenom's
13 products at the time. So other people in the company paid
14 attention to it, but I was really paying attention to our own
15 products.

16 Q. Your general belief is that the claimed inventions of the
17 '794 patent were successfully commercialized by Illumina in the
18 Golden Gate product; correct?

19 A. No, I don't think the claims in the '794 patent had
20 anything to do with the Golden Gate product.

21 Q. Okay. I would like to direct your attention to page 243,
22 lines 4 through 8, please.

23 A. This is in my deposition?

24 Q. July 24th.

25 A. Okay. Make sure I have the right pages.

1 **MR. WALTER:** I'll hand it to you.

2 **THE WITNESS:** I'm sorry. It's a different thing.

3 **MR. REINES:** Dr. Walter should be able to help you.

4 **THE WITNESS:** That one stopped at page 242, okay.

5 **MS. HABERNY:** Looking at which lines?

6 **MR. REINES:** 243, lines 4 through 8.

7 All right. Let's play it.

8 (Videotape was played but not reported.)

9 **BY MR. REINES**

10 **Q.** Now, you just testified right before I played that clip,
11 which reflected on your last answer -- you just testified that
12 you don't think that the claims have anything to do with the
13 Golden Gate assay.

14 Do you recall that?

15 **A.** Yeah, I don't think the claims of the '794 patent describe
16 the Golden Gate assay, yes.

17 **Q.** They don't describe it?

18 **A.** They don't. They don't -- well, they don't contain it.

19 **Q.** Okay. Claim 1 is practiced by the Golden Gate assay?

20 **A.** Ah, Claim 1 is a completely -- Claim 1 has nothing do with
21 allele-specific detection. It just has to do with the
22 detection of a minimum number of different sequences.

23 **Q.** I'd like to read your deposition. This is the July 28th,
24 2015 deposition, at page 63, line 15 through 19. July 28th,
25 2015.

1 **MS. HABERNY:** Give me a moment, please.

2 **MR. REINES:** Of course.

3 Okay. Okay. The question was:

4 "You testified that the Golden Gate, the method of
5 Claim 1, at least you believe is practiced by the
6 Golden Gate assay; correct?"

7 And your answer was:

8 "That's correct."

9 Do you see that?

10 **A.** Yes, I see that.

11 **Q.** That's what your transcript says?

12 **A.** Right.

13 **Q.** So when you were under oath in July in 2015, before this
14 trial, your testimony was that the Golden Gate assay invented
15 by Oliphant and Stuelpnagel was performed by Claim 1; correct?

16 **A.** Yeah. Obviously, you're reading my testimony, so I can't
17 contradict that. I'm trying to remember what my frame of mind
18 was at the time and why I said that.

19 **Q.** Okay.

20 **A.** Yeah.

21 **Q.** And you understood the scope of the claims at the time you
22 gave that testimony, didn't you?

23 **A.** I thought I did, yes.

24 **Q.** And in terms of the commercial success of the Golden Gate
25 assay -- that was -- was considerable; wasn't it?

1 A. I -- I -- I have no firsthand knowledge of that; but it
2 was -- I'm -- I understand that it was a successful product,
3 yeah.

4 Q. Okay. All right. Let's turn to Straus.

5 And actually, before I get to Straus, let me ask: These
6 patents -- the Patent Office has looked at these patents;
7 correct?

8 A. Of course.

9 Q. And with respect to the '430 patent, the Patent Office
10 looked at the -- well -- enablement question, and the written
11 description question that you're now challenging; is that
12 correct?

13 A. Yes.

14 Q. Okay. And with respect to Straus, the Patent Office
15 looked at that, too; didn't it?

16 A. Sure. But if the Patent Office were infallible, we
17 wouldn't be here; right?

18 Q. The Patent Office actually looked at it three different
19 times; didn't it?

20 A. I don't know how many times they looked at it.

21 Q. Okay. I'd like to show you Exhibit 719, 720, and 721.
22 And let's hand those out.

23 THE CLERK: Um-um. Tell me those numbers again.

24 MR. REINES: 719, 720, and 721.

25 THE CLERK: Okay. Thank you.

1 **MR. REINES:** Thank you.

2 **THE CLERK:** Sorry.

3 **MR. GINDLER:** Copy.

4 **MS. HABERNY:** Can we have a copy before Mr. Reines
5 asks any questions?

6 **THE WITNESS:** Actually, I have four different things
7 here. Perhaps that's not right. Okay.

8 I'm just supposed to have two. Oh.

9 **THE COURT:** Are there some for me, Tracy?

10 **THE CLERK:** No, not yet.

11 **MR. REINES:** We're trying to get them. Now there are
12 three of them, so --

13 (Whereupon a document was tendered to the Court.)

14 **THE CLERK:** Thank you.

15 **MS. HABERNY:** Your Honor, may we have a sidebar?

16 **THE COURT:** Sure.

17 (Whereupon the following proceedings were held at sidebar.).

18 **MS. HABERNY:** Your Honor, there's --

19 **THE COURT:** What's the pending question?

20 **MR. REINES:** I just handed them to him. I hadn't
21 asked him a question.

22 **THE COURT:** Before that, what was the --

23 **MR. REINES:** I had him confirm --

24 **MR. GINDLER:** The Patent Office has looked at this on
25 multiple occasions, was the question.

1 **MS. HABERNY:** The objection is to the way this is
2 proceeding. This has already been covered by the Court's
3 ruling. There's no --

4 **MR. REINES:** Let me be clear about what I'm doing.

5 **THE COURT:** What are you doing here?

6 **MR. REINES:** That is the right thing. I was just
7 going to go through and state what the nature of the decision
8 was. At the highest level there was a decision made on date X.
9 I can't do anything else with that.

10 **THE COURT:** No, that's just completely --

11 **MR. REINES:** Okay.

12 **THE COURT:** -- contrary to what we talked about.

13 **MR. REINES:** No, I thought there was an implication
14 that it wasn't considered by the Patent Office, because it
15 wasn't addressed in the direct. There was no objection to when
16 I just asked the question of him.

17 **THE COURT:** There should have been. There wasn't, so
18 the answer --

19 **MR. REINES:** There was no objection, all right. I'll
20 move on.

21 **THE COURT:** Okay.

22 (End of sidebar.)

23 (Proceedings were heard in the presence of the jury:)

24 **BY MR. REINES:**

25 **Q.** All right. Now, in terms of the Straus reference, let's

1 get right to that.

2 You never heard of Straus before this case?

3 I never heard of Straus before this case.

4 Q. And Straus was a patent application that never made it
5 past the application process?

6 A. I don't know what happened to it.

7 Q. Did you ever look to see whether it issued?

8 A. No, never looked.

9 Q. Okay. And did you ever ask Straus to come to the court?
10 Do you know if anyone ever asked him to come here and explain
11 what his invention was, or his attempt at --

12 A. I don't even know if he's alive.

13 Q. Okay. Now, let's talk about universal primers.

14 Do you recall that Dr. Quackenbush was describing the
15 universal primers as really important?

16 A. Yes.

17 Q. Okay. And you agree with that, that it's an important
18 requirement of the '794 patent?

19 A. Yes, I do.

20 Q. Okay. And now, you didn't present in direct any opinion
21 about there being identical universal primer in Straus; right?

22 A. I did. I talked about one amplification sequence, which
23 is Straus' term for a universal primer.

24 Q. But in terms of addressing the claim language "identical
25 universal primer," you'll agree that you never referred to

1 that?

2 **MS. HABERNY:** Your Honor, objection. Asked and
3 answered.

4 **THE WITNESS:** They don't use the same words.

5 **THE COURT:** Well, asked and answered. Objection is
6 overruled. So the answer can stand.

7 **BY MR. REINES**

8 **Q.** Now, your report didn't mention that Straus has identical
9 priming sites; right?

10 **A.** I don't remember. I think it did, actually.

11 **Q.** Do you not remember, or do you think it did?

12 **A.** No. Sorry. I don't remember my report verbatim, but I
13 believe it did mention universal priming sites.

14 **Q.** You think -- yeah, but it didn't mention identical
15 universal primers; right?

16 **A.** Well, identical universal means -- universal primer means
17 that they're identical, that there's one sequence.

18 **Q.** So your view is that in a process, universal primer and
19 identical universal primer is the same thing?

20 **A.** Yes.

21 **Q.** Okay.

22 **A.** Yeah. The "Identical" is redundant.

23 **Q.** Now, the nomenclature "universal primer" was standard at
24 the time of Straus; correct?

25 **A.** So I wish that nomenclature in biology and biochemistry

1 was standard, okay? Unfortunately, people use terms very
2 sloppily.

3 And both of these patents or patent applications contain
4 individualized terms that are not commonly used by people in
5 the field; and that's okay, as long as the patents define them,
6 which they did.

7 But we're faced with this conundrum that different patents
8 are using different non-standard terms for the same thing.

9 **Q.** Page 191, line 10 through 13. And I'll need to read this.
10 And this is the July 24th transcript?

11 **MS. HABERNY:** Would you give me a moment, please?

12 **MR. REINES:** Of course.

13 **THE WITNESS:** Yeah.

14 **MR. REINES:** So the question and answered was:

15 "Are you saying the nomenclature universal primers
16 was standard in the art by 2000?"

17 And your --

18 **THE WITNESS:** Sorry. Finish. Yeah.

19 **Q.** Please wait.

20 And the answer was:

21 "Yes, yes, absolutely."

22 Was that your testimony?

23 **A.** That was my testimony.

24 **Q.** That's the only question I have. We're limited on time.

25 Thank you.

1 Now, you have no explanation why Straus didn't use the
2 standard term "universal priming site," if that's exactly what
3 he was referring to; right?

4 **A.** I have no explanation, except that he also used very
5 peculiar terms for many other things in that patent. So he was
6 like inventing his own little world of nomenclature. I don't
7 know why he did that.

8 **Q.** But in terms of what you know, you don't have any
9 explanation at all -- and you didn't when I took your
10 deposition -- why Straus wouldn't have just used the term
11 "universal primer," since it's such a standard term?

12 **A.** I don't know why he didn't use standard terms in his
13 patent.

14 **Q.** All right. Now, your testimony was he should have used
15 "universal primer" instead of "amplification sequence;" right?

16 **A.** It would have made our task a lot simpler if he had.

17 **Q.** Okay. That's your view, is that he should have done that?

18 **A.** Yeah, yeah, yeah, yeah.

19 **Q.** Now, Straus defines almost everything; right?

20 **A.** That's a very broad statement. So it's hard for me to
21 agree with it, but he -- I don't remember seeing things that I
22 wish he had defined.

23 **Q.** Okay. That was your statement?

24 **A.** Yeah.

25 **Q.** Okay. And in paragraph 1000 -- paragraph 106, he defines

1 "amplification site," which is what you're now contending is
2 the universal primer; right?

3 A. That's correct.

4 Q. And you don't have an opinion that it's "identical
5 universal primer;" correct?

6 A. Okay.

7 Q. Dr. Cantor, you don't have that opinion? You haven't
8 given that, and you don't have it?

9 A. Okay. I need to clarify something.

10 Q. Sure.

11 A. Because Straus uses the term "amplification site" to cover
12 two entirely different things. He uses it, and he defines it
13 this way to include a primary binding site, as you would need
14 for PCR, and as relevant to the '794 patent; but he also uses
15 it to describe a site that would be recognized by enzymes, by
16 RNA polymerase, that replicate DNA, that amplify DNA, but that
17 don't use primers.

18 So he uses this one term to mean these two rather
19 different things, and that's why he uses this peculiar term.

20 Q. Please listen to my question.

21 You don't have an opinion that amplification sequence is
22 an identical universal primer in Straus; right?

23 A. So the term "amplification sequence" does not alone mean
24 universal primer; but when he says he's using one amplification
25 sequence, that, to me, means that he's using a universal

1 primer.

2 Q. There's nothing in the definition of "amplification
3 sequence" in the Straus application that suggests it is a
4 universal primer; correct? Would you agree with that?

5 A. That is correct.

6 Q. Okay. Now, what Straus actually says -- let's pull up
7 Straus, which is Trial Exhibit 1044, at 28.

8 (Document displayed.)

9 BY MR. REINES

10 Q. And do you see on paragraph 176 he refers to a very small
11 number of amplification sequences?

12 A. You'd have to show me.

13 Q. (Indicating).

14 A. Right. I see that.

15 Q. Okay. And you'll agree, Dr. Cantor, we have common ground
16 that paragraph 176 teaches using a small number of universal
17 primers?

18 A. That's exactly what the paragraph says.

19 Q. Now, whether or not paragraph 176 discloses universal
20 primers, that's not perfectly clear to you; is it?

21 A. Well, a small number can be one.

22 MR. REINES: Okay. No further questions.

23 THE COURT: Thank you. Anything further,
24 Ms. Haberny?

25 MS. HABERNY: Yes.

REDIRECT EXAMINATION

BY MS. HABERNY

Q. Dr. Cantor, you were asked a few questions about your opinions on the written description of the '430 patent.

Do you recall that?

A. Yes.

Q. And whether Dr. Rava had actual possession of the invention?

Do you recall that?

A. Yes.

Q. Is it your understanding that the standard for determining written description is what a person of ordinary skill would understand reading the patent as far as what the inventors possessed?

A. Yes.

MR. REINES: Objection. Leading, Your Honor.

MS. HABERNY: I just asked if that's --

Q. Would you tell the jury whether or not it's your understanding that for written description, you look at what a person of ordinary skill reading the patent would understand?

MR. REINES: Same objection.

THE COURT: Overruled. You may answer.

THE WITNESS: Yes.

BY MS. HABERNY

Q. And is there anything in the '430 patent that shows that

1 the named inventors had possession of the invention that's
2 claimed?

3 **A.** So anything -- I'm puzzled by your question.

4 **Q.** Does the '430 patent itself disclose any algorithms?

5 **A.** The '430 patent does not contain any tool for analyzing
6 the data, except for some of the references that it cites.

7 **Q.** And -- and does -- does the citation to those references
8 demonstrate that the inventors had possession of the non-random
9 approach and analysis that they claim in the patent?

10 **MR. REINES:** Objection. That's leading.

11 **THE COURT:** Overruled.

12 You may answer.

13 **THE WITNESS:** Yeah. So the references that are cited
14 are mostly whole-genome, random shotgun sequencing. I believe
15 there may be digital PCR references cited, as well, but those
16 are extreme opposites of this analysis. And -- and the patent
17 is right in the middle.

18 **BY MS. HABERNY:**

19 **Q.** Is there any evidence in the '430 patent, itself, that the
20 inventors actually possessed the invention that they claimed?

21 **A.** So they didn't reduce the invention to practice. It
22 didn't show a single example of the analysis of a fetal
23 trisomy.

24 **Q.** Thank you. Now, you were asked some questions -- or,
25 actually, your deposition was read from 2015, from a deposition

1 in which you were asked some questions about the Golden Gate
2 assay.

3 Do you recall that?

4 **A.** I recall discussing it a few minutes ago.

5 **MS. HABERNY:** Just a moment.

6 (Pause in proceedings.)

7 **BY MS. HABERNY**

8 **Q.** Do you recall that Mr. Reines read a portion of your
9 testimony from a deposition, that was on July 28th, 2015, about
10 the Golden Gate assay?

11 **A.** I recall that.

12 **Q.** Thank you. Now, I'd -- I'd like to read you another
13 portion of your deposition of that same deposition.

14 Question --

15 **THE COURT:** Where are you reading?

16 **MS. HABERNY:** Oh, I'm sorry. It's page 43, lines 16
17 through 44, line 19. Is it okay to go?

18 **MR. REINES:** I mean, I don't know what's the basis
19 for reading his deposition transcript.

20 **THE COURT:** What's the basis?

21 **MS. HABERNY:** I'm going to ask him about that to
22 refresh his recollection about his state of mind, where he said
23 he didn't understand his state of mind at the time.

24 **MR. REINES:** Doesn't go into the record, if that's
25 what the goal is.

1 **THE COURT:** Trying to complete the answer from
2 before, or --

3 **MS. HABERNY:** Can I show him the deposition to
4 refresh his recollection?

5 **THE COURT:** Oh, sure.

6 **MR. REINES:** It just doesn't go in the record.

7 **MS. HABERNY:** It's context for what was read, for
8 what Mr. Reines read.

9 **THE COURT:** Well, in that case, if that's what you're
10 offering it for, then you may do that.

11 **MS. HABERNY:** Okay.

12 "QUESTION: Your testimony is pretty clear that your
13 inference is that the '794 patent covers the
14 Golden Gate technology at Illumina; correct?

15 "ANSWER: So let me try to recapitulate what I think
16 I said to see if I contradict myself or not. I don't
17 know the full technical details of the Golden Gate
18 assay, okay? I know certain details of the
19 Golden Gate assay; and they include universal
20 primaries and ligation.

21 "And I have learned subsequently to my initial
22 exposure to the term Golden Gate assay that it
23 involves gap fill, that there are many different
24 kinds of gap fill, and I -- I don't actually know
25 factually what kind of gap fill the Golden Gate assay

1 uses.

2 "But if I, as an intelligent scientist in the field,
3 step back and ask if I had invented this assay, what
4 would I have used, then I could write something down.
5 But I have no certainty that that's what actually the
6 commercial product -- because I have, again, I have
7 never read the spec sheet of the commercial product."

8 Now, can you explain why you gave the answer to the
9 question that Mr. Reines read?

10 **THE WITNESS:** Yeah. So Claim 1 is very, very
11 general; it has lots of "comprisings" in it, okay? And so it's
12 very hard to -- to analyze something in the context of Claim 1
13 without really a thorough knowledge of what you're dealing
14 with.

15 And I, in fact, at that time, did not know the precise
16 details of how the Golden Gate assay worked. I merely knew
17 that it was looking at -- it was determining alleles.

18 **Q.** And were you speculating?

19 **A.** I was speculating at the time, yeah.

20 **Q.** Thank you.

21 Now, you were also asked some questions about the choice
22 of words that Dr. Straus used in his patent application, which
23 is your prior art reference.

24 Does anticipation require that the prior art reference use
25 the same words as the patent claims?

1 A. It does not require the same words. I think it could even
2 be a reference in Chinese; right?

3 Q. And is it your understanding that you can get a patent on
4 an old invention just by using new words to describe it?

5 A. I don't think you can get a patent on an old invention by
6 using new words, unless something slips up in the approval
7 process; right?

8 Q. And you also were asked some questions about universal
9 primers and amplification sequences.

10 Do you recall that?

11 A. I do.

12 Q. And what does Straus mean in the disclosure of one
13 amplification sequence?

14 A. Well, I think that's not what he said. I think what he
15 means by one amplification sequence is a single universal
16 sequence which, if it's a primer binding sequence, is a
17 universal primer; whereas, I indicated a few minutes ago,
18 because as Straus is using a more expanded version of this, it
19 also allows for other amplification systems that have a unique
20 recognition sequence, but that don't use a primer.

21 MS. HABERNY: Okay. Thank you. No more questions.

22 THE COURT: Thank you. Anything further?

23 MR. REINES: Yes, Your Honor.
24
25

RECROSS-EXAMINATION

BY MR. REINES

Q. You just testified that unless something slipped up in the process, do you recall that?

A. Yes.

Q. Okay. And just to reiterate what was said before, this was looked at three different times by the Patent Office?

MS. HABERNY: Objection, Your Honor.

MR. REINES: Your Honor, he just said, "unless it slipped up during the Patent Office procedure." He invoked it.

MS. HABERNY: Your Honor, may we sidebar?

THE COURT: I'm going to sustain the objection and disallow the question.

BY MR. REINES

Q. Okay. You don't dispute -- well, first of all, you know Figure 13 from the '794 patent? That's something in preparing for the case you're familiar with?

A. I have looked at Figure 13, yes.

Q. And you were here when Dr. Stuelpnagel said he invented Figure 13, and that was Golden Gate?

A. I was here when he invented that, and I agree that Figure 13 is the Golden Gate assay.

Q. And you also recall Dr. Oliphant testifying quite clearly that the description of Figure 13 described his invention of Golden Gate as well; right?

1 A. I don't remember that now. But, you know, it's certainly
2 consistent.

3 Q. Okay. And you'll agree that Figure 13 is covered by
4 Claim 19 of the '794 patent?

5 A. No, I don't agree. I know that at one time I thought that
6 was the case. But as I've studied this much more carefully,
7 that definitely is not covered by Claim 19.

8 Q. And your deposition was taken in July of 2017?

9 A. I trust you on the date.

10 Q. And you studied for it for 40 hours?

11 A. I have looked at this again subsequently, and I realized
12 that I did make a mistake in that deposition. And that
13 Claim 19 definitely does not cover the Golden Gate.

14 Mind you, Claim 19 is not asserted against us. It was not
15 something I had studied in detail at the time. So when you
16 asked me about it at the time, I was sort of answering off the
17 cuff, and I was wrong.

18 Q. At the time you had an opinion on inventorship; correct?

19 A. Ah --

20 Q. When you say you didn't study it, you had an opinion on
21 whether --

22 A. I had an opinion on inventorship, but I did not study
23 Claim 19.

24 Q. And you're not presenting that opinion here; right?

25 A. No.

1 Q. Okay. I'd like to play page 47, line 12 through 48, line
2 2. It's a video clip 22.

3 THE COURT: Of the?

4 MR. REINES: Sorry. The recent deposition in the
5 summer, July 24th, 2017.

6 (Videotape was played but not reported.)

7 MR. REINES: No further questions.

8 THE COURT: Thank you.

9 MS. HABERNY: Nothing further.

10 THE COURT: Thank you very much, sir. You may step
11 down.

12 MS. RUSSELL: May I introduce it to the jury?

13 The next witness will be appearing under deposition video.
14 It's under four minutes. I can introduce it to the jury.

15 THE COURT: If it's under four minutes, then we'll do
16 that now, and then go to lunch.

17 THE CLERK: Are we going to mark it as an exhibit?

18 THE COURT: It won't be reported by the court
19 reporter, but it will be marked as an exhibit.

20 THE CLERK: And not sent to the jury?

21 MS. RUSSELL: It will just -- yeah -- be played.

22 Is that a video?

23 THE CLERK: So do we --

24 MS. RUSSELL: I have the transcript.

25 THE CLERK: Well, what I'd like is a number. And I

1 want to find your binders.

2 **MR. GINDLER:** We'll be introducing the testimony of
3 Mr. Crane Harris.

4 **THE CLERK:** Crane. Spell that.

5 **MR. GINDLER:** C-R-A-N-E, last name, Harris. And it
6 will be done by playing excerpts from his deposition for the
7 jury.

8 **THE CLERK:** And we're going to get a DVD with the
9 excerpts only and a number.

10 And let me just give you a number real quick for the
11 record. So that will be 718.

12 (Trial Exhibit 718 marked for identification)

13 **THE COURT:** Are there any objections to the video?

14 **MR. REINES:** No. We've worked together on this.

15 **THE COURT:** Okay. So what this is, ladies and
16 gentlemen, Mr. Harris evidently gave a deposition. It was
17 videotaped. These are four minutes' worth of excerpts from
18 that deposition. Both the parties have agreed it may be played
19 in lieu of his live testimony. So he won't come in alive -- he
20 is alive. He won't come here.

21 (Laughter)

22 **MR. REINES:** He's alive.

23 **THE COURT:** And you may treat this testimony as if it
24 were given here in open court.

25 **MS. RUSSELL:** May I introduce the date of the

1 deposition.

2 So you're about to watch an excerpt of a video deposition
3 of Mr. Crane Harris. The deposition was taken on March 15th,
4 of 2017. And at the time of the deposition Mr. Crane Harris
5 was an employee at Illumina.

6 (Videotape was played but not reported.)

7 **THE COURT:** Is that it?

8 All right. At this point, ladies and gentlemen, we'll
9 take our lunch recess.

10 If you would be ready to come back, please, at 12:30.

11 In the meantime, please don't discuss this matter with
12 each other or anyone else. Don't make up your minds. You have
13 not heard all of the evidence yet.

14 (Proceedings were heard outside the presence of the jury:)

15 **THE CLERK:** I'm sorry. Go ahead. I thought you were
16 going to be done.

17 **THE COURT:** Who's next?

18 **MS. CURRAN:** Jean Yee, on behalf of Ariosa
19 Diagnostics.

20 **MR. REINES:** Your Honor, that's the issue with the
21 motion that we filed, if the Court had an opportunity to look
22 at it. This is on the -- the reimbursement.

23 **THE COURT:** Yes, that motion is denied.

24 **MR. REINES:** It's denied? I'm sorry?

25 **THE COURT:** Denied.

1 **MR. REINES:** Yeah, okay.

2 **THE CLERK:** So what I'd need you guys to do is mark
3 the drawings, and then I need the video clip.

4 **MR. GINDLER:** Yes, of course.

5 **THE COURT:** And I think that that's it.

6 (Luncheon recess was taken at 11:49 a.m.)

7 **AFTERNOON SESSION**

12:30 p.m.

8 (Proceedings were heard outside the presence of the jury:)

9 **THE CLERK:** So who wants to -- do you want me to do
10 it? I'll do it. I don't care.

11 So 1660 is an amplicon. 1661 is the digested amplicon.
12 1662 and 1663 are drawings. And 1664 is the poster board.

13 (Trial Exhibits 1660-1664 marked for identification)

14 (Whereupon a document was tendered to the Court.)

15 **THE COURT:** So those were all just marked; right?

16 **THE CLERK:** Just ID's.

17 **THE COURT:** Are we ready?

18 **MS. CURRAN:** Yes.

19 **MR. REINES:** Yes.

20 **THE COURT:** Okay.

21 (Proceedings were heard in the presence of the jury:)

22 **THE COURT:** All right. The defendant may call its
23 next witness.

24 **MS. CURRAN:** Ariosa calls Jean Yee.

25 **THE CLERK:** You can go ahead and take a seat.

1 **THE WITNESS:** Thank you.

2 **THE CLERK:** I'm going to take your picture. Focus.

3 It kind of seems blurry right now.

4 Raise your right hand.

5 **JEAN YEE,**

6 called as a witness for the Defendants, having been duly sworn,
7 testified as follows:

8 **THE WITNESS:** Yes.

9 **THE CLERK:** Okay. Why don't you pull that
10 microphone.

11 State your full name for the record.

12 **THE WITNESS:** My name is Jean Wah Yee.

13 **THE CLERK:** Spell your last name.

14 **THE WITNESS:** My last name is Y-E-E.

15 **THE CLERK:** And Jean is with a "J" right?

16 **THE WITNESS:** Yes, it's J-E-A-N.

17 **THE CLERK:** Thank you.

18 **DIRECT EXAMINATION**

19 **BY MS. CURRAN**

20 **Q.** Good afternoon, Ms. Yee.

21 Could you introduce yourself to the ladies and gentlemen
22 of the jury?

23 **A.** Hi. My name is Jean Yee. I'm currently the Head of
24 Finance for Ariosa Diagnostics.

25 **Q.** And how long have you worked at Ariosa Diagnostics?

1 A. I've been at Ariosa for about six years.

2 Q. And could you give the jury an overview of the career path
3 that you took to ultimately end up at Ariosa Diagnostics?

4 A. Sure. So I went to school at U.C. Santa Barbara. After
5 graduating, I moved back up to the Bay Area, started working
6 for a local public accounting firm. So I was in public
7 accounting for a few years. After that I joined a company
8 called Affymetrix in Santa Clara as a revenue accountant; and
9 from there, over the course of about 13 years, worked my way up
10 to the Director of Finance.

11 Q. And what drew you to join Ariosa?

12 A. So after I left Affy, I took some time off of work --
13 about six months -- and I went to join Ariosa initially as a
14 consultant.

15 One of my former managers had called me up. He needed
16 help putting together a budget, and wanted to know if I'd be
17 interested. So I joined as a consultant to put together a
18 budget for the company.

19 Q. And what kept you at Ariosa?

20 A. So I was a consultant for just a couple of months; and
21 then the company decided that they needed to put in an
22 accounting system, and asked if I would be willing to stay on
23 and help put that in.

24 So part of it was a career opportunity, but part of it
25 was -- you know, by then I'd met the team, and I really enjoyed

1 the people on the team there. And then there was also the
2 opportunity just to be a part of a team that wanted to and had
3 the ability to make a difference in women's lives, and, you
4 know, prenatal care.

5 **Q.** So you mentioned you worked on the budget and putting in
6 an accounting system.

7 Can you give the jury an overview of your other
8 responsibilities during your time at Ariosa?

9 **A.** Sure. So aside from forecasting and budgeting and the
10 financial system, I also participated in reviewing business
11 processes, business processes and improvements.

12 In my current role as Head of Finance, there is not only
13 the finance aspect, but also the accounting aspect. So the
14 accounting team is the group that takes care of keeping our
15 books.

16 **Q.** And when you arrived at Ariosa, did you gain a sense of
17 the company's key goals?

18 **A.** Yes. I mean, the key goal was to make a non-invasive
19 prenatal test affordable for all pregnant women.

20 **Q.** And in your role, did you help to work towards achieving
21 these goals?

22 **A.** Yes. When -- you know, as part of looking at budgets and
23 forecasts, we're always looking at how we should be spending
24 our money, you know, where can we cut costs, where it makes
25 sense, how do we do things better, more efficiently.

1 Q. And as you were working with the team to achieve these
2 goals, can you give some examples of the processes you went
3 through?

4 A. Definitely part of the budgeting process; but I would say
5 one of the things when I joined the company was, you know,
6 we're located in south San Jose, so it's a little bit more
7 affordable in the Bay Area in terms of rent, as opposed to say
8 in Palo Alto.

9 We also were looking at -- we got things like free
10 furniture in an effort to cut down costs. So we're always
11 looking to spend money wisely.

12 The other part in looking at the cost of sales, you know,
13 how much it cost to develop our assay, was we were always
14 looking at are there things that we can reduce costs and still
15 be as effective.

16 You know, one of the examples I can give is when we first
17 launched our test in the U.S., the blood collection box
18 included two tubes that used to collect blood. Each one of
19 those tubes is about \$7, \$8. That was definitely an area where
20 we could look to reduced costs. We ended up developing our own
21 tube, or rather a tube that somebody else had developed, but
22 our own preservative. And today that pair of tubes costs us
23 about a dollar.

24 Q. Okay. And you mentioned you help oversee Ariosa's
25 accounting.

1 In your role, do you keep track of payments that Ariosa
2 makes?

3 A. Yes.

4 Q. And does that include payments made to suppliers?

5 A. Yes, it does.

6 Q. In the 2012/2013 time frame, would you have been involved
7 in reviewing Supply Agreement?

8 A. Yes.

9 Q. And did Ariosa need to acquire supplies to run and develop
10 its tests?

11 A. Yes, we did.

12 Q. And could you provide some examples of what kinds of
13 supplies you purchased?

14 A. So to run our test in the lab, we definitely needed
15 equipment, so a variety of lab equipment. You also need things
16 like lab coats and gloves, and you need chemicals and reagents,
17 and so forth.

18 Q. And when a bill comes in, say for one of the things you
19 just mentioned, what process does your team go through?

20 A. So when we receive a bill in our accounting group, we log
21 that invoice into our accounting system. Before we pay it,
22 we'll check with our receiving group or with the end user to
23 make sure that they received what they ordered. It could be a
24 good or a service. Once they've confirmed that, we'll take a
25 look at when the bill is due, and as it gets closer, we'll cut

1 a check and pay that bill.

2 Q. You mentioned logging into a system. Can you go into that
3 system and pull information about what you've paid to a
4 particular vendor?

5 A. Yes.

6 Q. And was Illumina one of Ariosa's suppliers?

7 A. Yes.

8 Q. And are you familiar with the Illumina/Ariosa Supply
9 Agreement?

10 A. Yes.

11 Q. Do you know if Ariosa made payments to Illumina under this
12 agreement?

13 A. Yes, we did.

14 Q. And how much did Ariosa pay Illumina under that agreement?

15 MR. REINES: Objection, Your Honor. That's
16 best-evidence rule. The best evidence clearly is the actual
17 accounting documents, not witness testimony.

18 MS. CURRAN: She will not be testifying to prove the
19 content of any sort of accounting document. They log their
20 information into a system. She would have to pull the
21 information out of the system, and on her own independent
22 analysis to arrive at this figure, which she's happy to
23 explain.

24 MR. REINES: It can't be that they can put in a
25 number without any documentation to back up what the amount is.

1 How are we going to cross-examine? It's a best evidence
2 violation.

3 **THE COURT:** Has the -- that's overruled.

4 Has the underlying documentation been provided to the
5 other side?

6 **MS. CURRAN:** I mean, obviously they have access to
7 their own internal records, which would include what Ariosa has
8 paid them. We have not provided them with this particular
9 analysis. We would be happy to do so.

10 **THE COURT:** All right. You will be ordered to do so.

11 **MS. CURRAN:** Okay. Thank you, Your Honor.

12 **THE COURT:** But the objection is overruled.

13 **MS. CURRAN:** Great.

14 **Q.** So how much did Ariosa pay Illumina under that agreement?

15 **A.** So from 2012 to 2014, we paid about 14.4 million.

16 And that would be based on purchases made by our lab, and
17 excluding any R & D purchases.

18 **BY MS. CURRAN**

19 **Q.** And how did you agree -- arrive at the \$14.4 million
20 figure that you just testified to?

21 **A.** So I was able to pull a query of the transactions, the
22 bills that we've received from Illumina, and I totaled those
23 up, excluding, again, the R & D purchases.

24 **Q.** And do you recall submitting a declaration in this case
25 back in September?

1 A. Yes.

2 Q. And do you remember that you testified that Ariosa paid
3 Illumina about \$17.6 million under the Sale and Supply
4 Agreement?

5 A. Yes.

6 Q. Why is the \$14.4 million figure that you've just testified
7 to different than the number in your declaration?

8 A. So the 14.4 million is from 2012 to 2014; and, again, it
9 excludes our R & D payments.

10 The 17.6 million covers 2012 to 2015; and it includes
11 payments, basically royalties that we had to pay on tests that
12 we ran on the Illumina platform, for which we subsequently
13 received payment. But it also includes a number of R & D
14 purchases that probably were not under the Sale and Supply
15 Agreement, in retrospect.

16 Q. Now, you mentioned you did some analysis to arrive at your
17 \$14.4 million figure.

18 Did you do an analysis back when you submitted your
19 declaration?

20 A. Yes.

21 Q. And what makes your testimony today different?

22 A. In going back over the 17.6 million, in retrospect, I
23 overlooked some of those purchases were for R & D.

24 MS. CURRAN: Thank you. I pass the witness.

25 THE COURT: Thank you.

1 **MR. REINES:** Thank you.

2 **THE COURT:** Mr. Reines?

3 **MR. REINES:** Sure. Thank you, Your Honor.

4 **CROSS-EXAMINATION**

5 **BY MR. REINES:**

6 **Q.** So to come up with the \$17 million number that you
7 originally had --

8 Do you recall that?

9 **A.** The 17.6?

10 **Q.** Yes.

11 **A.** Yes.

12 **Q.** Did you look at documents?

13 **A.** I pulled transactions. I did a query from our accounting
14 system.

15 **Q.** Sure. You looked at electronic documents?

16 **A.** Electronic records?

17 **Q.** Yeah, records, documents.

18 And when you did the \$14 million calculation, did you look
19 up electronic records?

20 **A.** Yes.

21 **Q.** Okay. Did you provide any to counsel?

22 **A.** No.

23 **Q.** Do you have an itemization of what those products were
24 that you're -- that you're identifying within the \$14 million?

25 **A.** Not off the top of my head.

1 Q. Do you know what model numbers they are relative to, the
2 model numbers of the products under the Supply Agreement?

3 A. Not off the top of my head.

4 Q. Did you ever do a comparison of the specific products
5 purchased under the Supply Agreement with the specific list
6 against the product numbers in your electronic documentation?

7 A. The approach that I took was to take a look at all of the
8 materials that were purchased by our lab groups, and assume
9 that those were purchased under the terms of the Sale and
10 Supply Agreement.

11 Q. Okay. So you didn't actually see -- you understand
12 there's a finite list of products that are actually authorized
13 to be sold and purchased under the Supply Agreement?

14 A. Yes.

15 Q. And you understand there are other purchases that go on
16 that aren't under the Supply Agreement?

17 A. Yes.

18 Q. And you didn't do any comparison to determine one from the
19 other?

20 A. I did take a look; but, again, I took a high-level
21 approach and assumed that in the normal course of business what
22 our lab was purchasing would be what was offered under the
23 terms of the Supply Agreement.

24 Q. You just made an assumption. You didn't do an analysis;
25 correct?

1 A. I did take a quick look at it.

2 Q. When you say you took a quick look at it, did you compare
3 the product serial numbers, whatever they are, I don't know
4 what they call them, but the serial numbers, and you checked
5 the actual products in the Supply Agreement.

6 Did you do a systematic analysis?

7 A. I did a spot analysis.

8 Q. Okay. And did you exclude anything as a result of that?

9 A. I excluded our R & D purchases.

10 Q. Oh, okay. But none of your commercial purchases for your
11 lab?

12 A. No commercial purchases.

13 Q. Okay. And now with respect to the \$14 million -- most of
14 that was consumables; correct?

15 A. Correct.

16 Q. Okay. And those consumables were used by Roche or Ariosa?

17 A. Yes, they were purchased for our lab.

18 Q. And they're -- do you know -- would you say it was
19 80 percent of that was consumables, that amount, that
20 \$14 million?

21 A. I don't know that off the top of my head.

22 Q. Do you have any idea?

23 A. Most of it was consumables, but I don't have an estimate
24 for you.

25 Q. Okay. And your understanding is Ariosa used the -- bought

1 the consumables under the Supply Agreement, used them, and sold
2 tests, and made revenue; correct?

3 A. Correct.

4 Q. And you understand that Ariosa is now saying it wants that
5 money back?

6 A. Yes.

7 Q. One other question.

8 In terms of the sequencers, do you know -- the sequencers
9 that are purchased -- I guess it's not most of it, because most
10 of it is consumables, but whatever remained were actual
11 sequencers -- do you know where those are? Are those being
12 used by Roche now?

13 A. I don't know where they are all physically located today.

14 Q. Okay. Do you know that they're being used by Roche, or
15 you don't know that?

16 A. I'm not sure.

17 Q. And you're an employee of Roche now?

18 A. I am.

19 Q. You introduced yourself as Ariosa.

20 Does Ariosa still exist, to your knowledge?

21 A. Ariosa still does exist.

22 Q. But you're a Roche employee?

23 A. I'm an employee of Roche, and Ariosa is wholly owned by
24 Roche.

25 Q. Okay. And with respect to -- I guess I have more than

1 one. I apologize for that. I'll be quick.

2 In terms of the depreciation of the sequencers, do you
3 know that that's normally around a three-year life cycle?

4 **A.** Yes.

5 **Q.** Okay. And in terms of, again, what was done with the
6 sequencers at the end, do you know what use Ariosa-Roche made
7 after, at the end of 2014, with the sequencers they'd
8 purchased?

9 **A.** If any were still in usable condition, our R & D group may
10 have used them.

11 **Q.** When you say, "may," you believe that's what happened;
12 correct?

13 **A.** I believe that they had an interest in using them. I'm
14 not sure if they actually used them.

15 **Q.** Okay. And at that point the research group was the -- was
16 the large Roche entity?

17 **A.** Ariosa also has a research group.

18 **Q.** Okay. Which group wanted to use the sequencers; do you
19 know?

20 **A.** Ariosa -- the Ariosa R & D team expressed an interest.

21 **MR. REINES:** Well, thank you for coming down today.

22 **THE WITNESS:** You're welcome.

23 **THE COURT:** Ms. Curran.

24 **REDIRECT EXAMINATION**

25

1 BY MS. CURRAN

2 Q. When Ariosa purchased the consumables, was it expecting to
3 come back and be sued by Illumina for its use of those
4 consumables?

5 MR. REINES: Objection. Lack of foundation.

6 THE WITNESS: No.

7 THE COURT: Sustained.

8 BY MS. CURRAN

9 Q. Now, counsel just asked you about sequencers potentially
10 being in use but your R & D department.

11 When Ariosa purchased the sequencers, do you have
12 knowledge of whether those were meant to be used commercially
13 or in research?

14 A. We purchased the sequencers with the intent that they
15 would be used in our lab.

16 MS. CURRAN: Thank you. Nothing further.

17 MR. REINES: Nothing further, Your Honor. Thank you.

18 THE COURT: Thank you very much, ma'am. Your
19 excused.

20 THE WITNESS: Thank you.

21 THE COURT: All right. Defendant may call its next
22 witness.

23 MS. GLASSER: Ariosa calls Dr. Ryan Sullivan.

24 THE CLERK: You can be seated.

25 Is that for the Judge or --

1 (Whereupon a document was tendered to the Court.)

2 **THE CLERK:** I'm just going to take your picture
3 really quick, if I can get my camera to -- picking up the
4 camera.

5 Raise your right hand.

6 **RYAN MICHAEL SULLIVAN,**
7 called as a witness for the Defendants, having been duly sworn,
8 testified as follows:

9 **THE WITNESS:** I do.

10 **THE CLERK:** Thank you.

11 Please state your full name for the record.

12 **THE WITNESS:** Ryan Michael Sullivan.

13 **DIRECT EXAMINATION**

14 **BY MS. GLASSER**

15 **Q.** Good afternoon, Dr. Sullivan, and ladies and gentlemen of
16 the jury.

17 **A.** Good afternoon.

18 **Q.** Dr. Sullivan, could you give the jury an overview of your
19 title and background?

20 **A.** Certainly. So I am the Chief Executive Officer of
21 Intensity Corporation. We provide services -- business
22 analytic services -- in the areas of economics, finance, and
23 statistics.

24 **Q.** And what is your educational background, briefly?

25 **A.** I earned a bachelor's degree, a master's degree, and a

1 Ph.D., all in Economics, and all from the University of
2 California in San Diego.

3 **Q.** Aside from San Diego being a lovely place to live, was
4 there something in particular that drew you to the program at
5 U.C. San Diego for your Economics Ph.D.?

6 **A.** Yes, a couple of items.

7 First off, UCSD and the Economics Department there is
8 world renowned for its research and quantitative economics and
9 mathematical economics. It's typically ranked in the top one,
10 two, or three schools in the nation; and it also gave me an
11 opportunity to work with two Nobel Prize Laureates directly,
12 which I found to be very helpful; very interesting.

13 **Q.** Have you had any experience specifically with intellectual
14 property licensing?

15 **A.** Yes. I have been providing professional economic services
16 for over 25 years, including valuation, licensing, and
17 monetization of intellectual property.

18 **Q.** And have you ever had the opportunity before today to
19 provide testimony to a jury in a case relating to intellectual
20 property issues?

21 **A.** Yes, on multiple occasions.

22 **MS. GLASSER:** Your Honor, I'd proffer Dr. Sullivan as
23 a damages expert.

24 **THE COURT:** Do you wish to *voir dire*?

25 **MR. COX:** No, Your Honor.

1 **THE COURT:** Thank you. You may proceed.

2 **BY MS. GLASSER**

3 **Q.** Dr. Sullivan, have you had the opportunity to review
4 documents and records produced by the parties in this case?

5 **A.** Yes, I have reviewed voluminous documents, testimony,
6 data, research information; a very large collection of
7 materials.

8 **Q.** And were you here in court yesterday for the testimony of
9 Dr. Kenneth Song?

10 **A.** Yes, I was.

11 **Q.** Have you had the opportunity to review any of the other
12 testimony in this case?

13 **A.** Yes, I have had access and read all of the trial
14 transcripts.

15 **Q.** And do you have an understanding at a high level of the
16 different categories of harm that Ariosa believes it suffered
17 due to the events of April 24th and 25th, 2014?

18 **A.** Yes, I do.

19 **Q.** We're looking at a slide deck up on the screen.

20 Is this part of what you prepared to help illustrate your
21 testimony today?

22 **A.** Yes, indeed.

23 **Q.** And I'm holding the clicker here; but of course I can act
24 as your clicker if you want me to go forward and backward.

25 Just let me know.

1 A. Forward one would be perfect.

2 Q. Can you describe the categories of harm to Ariosa that you
3 investigated?

4 A. Yes. So first off, the breach of contract and the breach
5 of Covenant of Good Faith and Fair Dealing, that caused Ariosa
6 to cancel their initial public offering, the IPO. That had a
7 couple of direct effects.

8 So first off, they had already spent approximately
9 \$2.9 million in hard costs to prepare for the IPO. So these
10 would be for accountants, bankers, and attorneys in helping to
11 set up the IPO. So those costs were wasted as a result of not
12 being able to move forward with the IPO.

13 Secondly, is that the IPO was expected to generate between
14 52 million and \$60 million in proceeds, that would go in to
15 Ariosa. The harm is not just the money that they would have
16 received, but it's the return on what they would have been able
17 to do with those funds.

18 So in the S-1 filing with the Securities and Exchange
19 Commission, Ariosa set forth what it is that they were going to
20 do with those funds. And in particular, significant amounts
21 were going to go to building up their sales and marketing
22 infrastructure, having more salespeople on the ground going out
23 meeting with physicians, insurance carriers, other geographies,
24 going into the international area. So this really would have
25 fueled their -- their financial growth.

1 It also would have enabled them to improve their corporate
2 infrastructure, and to continue along with their R & D.

3 **Q.** And you also note on the slide "accelerated switch to
4 microarray."

5 Could you speak about that as well?

6 **A.** Yes. Dr. Song had mentioned yesterday that the -- that
7 the breaches by Illumina -- that caused them to very quickly
8 and very effectively move over to accelerating the transition
9 to the microarray. That caused them not only to focus the
10 resources on the microarray and accelerate those costs, but
11 also then to divert their energies away from other R & D and
12 other efforts that they would be undertaking.

13 **Q.** Your slide also refers to roadblocks with partnerships
14 with distributors.

15 What do you mean by that?

16 **A.** In particular, in the early days of the marketplace for
17 NIPT, many of the providers such as Ariosa were working with
18 distributors, laboratories such as LabCorp and Quest, for
19 example.

20 And at this point in time, right at the IPO, Ariosa was
21 engaged in discussions and negotiations with some of these
22 partners, and the lawsuit caused those negotiations to fail,
23 such that then Ariosa was deprived of having that partnership
24 that would allow them to distribute their tests in a much more
25 broad fashion.

1 Q. Now, just turning back briefly to the first point you
2 mentioned about the 52 to \$60 million, could Ariosa have
3 reasonably achieved that through an alternative method such as
4 a loan?

5 A. No, that would not be feasible; and we know this for a
6 couple reasons.

7 First off, the lawsuit caused Ariosa to cancel the IPO.
8 That means that it caused them to have an inability to acquire
9 financing, whether that be through an IPO in the public
10 financing, or through debt financing such as a loan.

11 Second of all, we know that Ariosa did not pursue debt
12 financing. Clearly, if this was something that could have been
13 addressed simply by going and getting a loan, they would have
14 done so.

15 Third, for a company the size of Ariosa at that time, a
16 loan of on the order of 52 to \$60 million would not be
17 feasible.

18 Q. Did you perform any calculations to quantify the financial
19 impact to Ariosa of not having the IPO proceeds and the other
20 events arising out of Illumina's conduct?

21 A. Yes. I performed multiple analyses.

22 And on the next slide -- thank you -- you'll see that I
23 performed a forecast analysis, a marketplace analysis, and a
24 valuation analysis.

25 Q. And let's go through your forecast analysis first.

1 Can you describe -- what are we looking at here on this
2 slide demonstrative 6.4?

3 **A.** This is a chart depicting actual revenue and forecasted
4 revenue for Ariosa.

5 So you can see the green line towards the bottom -- that's
6 their actual revenue starting from the second quarter of 2012,
7 when Harmony™ was introduced, going out through the end of
8 2016.

9 You'll see that right at the second quarter of 2014, which
10 is when the breaches occurred, that that's where they're -- the
11 actual revenue just starts to come off of its trajectory, and
12 then starts to turn and come down.

13 And right at that time, Ariosa performed multiple
14 forecasts of what they expected their revenue to be out through
15 2016.

16 And these are forecasts that reflected the ability to move
17 forward with the IPO; and you can see that in blue. And that's
18 what they were forecasting their revenue to be.

19 There's a couple of interesting points here, literally.
20 One of them you'll see in the fourth quarter of 2015, where
21 there's a blip up, and then you'll also see the blip up in the
22 fourth quarter 2016. And that's because there are -- there's
23 seasonality with respect to the flow of revenue that comes into
24 these companies, because of the contracts with payers. So
25 these are seasonal or quarterly type aspects that you see

1 throughout the data.

2 **Q.** Now, using this revenue data and forecast data we just
3 looked at, how did you go about calculating the harm to Ariosa?

4 **A.** Well, it's in two steps. So first off, looking at the
5 difference between the actual revenue and the forecasted
6 revenue, provides the difference in revenue or financial
7 performance; but of course the harm isn't just the revenue,
8 because any additional revenue would also involve additional
9 cost to be incurred to be able to secure those revenue.

10 So here, on this slide, I'm demonstrating that when you
11 look at the difference of those revenue and account for the
12 incremental cost, that the total difference or the total harm
13 is \$88.5 million.

14 And in particular, you can see that in calendar year 2014,
15 that amount is \$3.4 million.

16 For 2015, the amount is \$34.9 million.

17 And then in the final year of 2016, the harm is
18 \$50.2 million.

19 **Q.** And why do you see the harm continuing to increase over
20 time?

21 **A.** The IPO was positioned at a pivotal time for Ariosa. They
22 had just turned a corner to becoming just barely profitable.
23 And they had already experienced some of the most rapid growth
24 in the industry; and they were poised to be able to have
25 continuing growth going forward. And thus, the harm is

1 something that cannot be rectified at this point in terms of
2 their sales and financial performance.

3 Q. You referred to a marketplace analysis.

4 Can you walk us through that, as well?

5 A. Yes. So what I showed you a moment ago was a forecast.
6 And, of course, forecasts are forward looking. And while
7 Ariosa was in an excellent position to forecast their revenue,
8 because they knew their business, their customers in the
9 marketplace better than anybody, it is still a forecast, and
10 forecasts are not perfect.

11 So what I did is I looked at the marketplace with
12 hindsight. So how did the marketplace actually evolve? How
13 did the growth actually occur during this period of time? And
14 I looked at the -- the financial performance and sales
15 performance of others, such as Sequenom, Natera, and Verinata.
16 I also looked at Illumina, and the global NIPT marketplace.

17 And when I do the very same analysis I did for the
18 forecast using the market data -- the actual data -- using
19 hindsight, the number is actually a bit higher; it's
20 \$106 million of calculated harm.

21 Q. And so what does this marketplace analysis indicate to you
22 about your forecast calculation?

23 A. It demonstrates that the forecast analysis yields an
24 answer that is reasonable and conservative.

25 Q. Now, did you perform any other analysis to try to again

1 corroborate that your forecast conclusion was reasonable?

2 **A.** Yes. So I also performed a valuation analysis. And what
3 I did here is I compared -- I calculated the value of the
4 outstanding shares of stock in Ariosa, and I calculated the
5 value with the IPO, and I compared it to the value without the
6 IPO, so I could look at the difference in value of those shares
7 outstanding.

8 **Q.** And before we dig into the numbers a little bit, what is
9 the purpose of looking at the value of the company?

10 What does that actually tell you about the out-of-pocket
11 dollars?

12 **A.** The value of the company reflects the financial
13 performance of the company. It's a way for us to gain insight
14 into its financial performance.

15 Put another way, it's a way for us to measure the
16 financial performance of Ariosa by looking at the company
17 value.

18 **Q.** How did you calculate the value with IPO figure?

19 **A.** So this is really based upon two inputs. The first is the
20 price per share that was set forth in the S-1 filing, which was
21 between 16 and \$18 per share. This is reflected in the
22 midpoint there of \$17 per share. The second piece of
23 accounting for what's known as the IPO discount of 20 percent.

24 So the -- most IPOs are priced at what's considered a
25 discount-to-market value; and empirical research that's been

1 published in many different academic journals has investigated
2 this to see that, on average, it's about 20 percent.

3 I also looked at a collection of just over 60 biotech
4 companies that also had IPOs in the 2013/14 time frame. There,
5 the average discount was 21 percent.

6 And the bankers, JPMorgan, with Ariosa, had calculated it
7 out to be 20 percent. So what I used was 20 percent on that
8 basis.

9 **Q.** So that's the \$281 million figure.

10 Then how did you go about comparing that to the actual
11 value?

12 **A.** So the actual value is based upon a valuation report that
13 was provided by Silicon Valley Bank Analytics.

14 This was a valuation that was performed to value the
15 equity -- the stock -- in Ariosa; because at that point in time
16 Ariosa was not a publicly traded company, so there were not
17 daily market transactions to inform what the value of the
18 equity would be.

19 So Silicon Valley Bank was engaged at multiple points
20 across the Ariosa history to be able to calculate what that
21 value would be for both tax and accounting purposes, as well as
22 for business decision making purposes at Ariosa.

23 **Q.** Now, to be clear, this SVB analysis that you relied
24 upon -- was this something that was performed just for
25 litigation, or was it performed in the ordinary course of

1 business?

2 **A.** It was for the ordinary course of business, unrelated to
3 the litigation.

4 **Q.** And what does your valuation analysis tell you about the
5 forecast analysis that you presented?

6 **A.** So the valuation analysis indicates that the harm is
7 approximately \$99.5 million. I view this as reasonable, for
8 some of the reasons that I've indicated.

9 But also I should add that, you know, on the pricing of
10 the IPO, which was supposed to be between 16 and \$18 -- during
11 this period of time, I looked at these same just over 60
12 biotech IPO offerings during this time frame, and 76 percent of
13 them actually, you know, met or exceeded their range, which is
14 another reason that explains why -- why this is reasonable.

15 This amount further, in my view, demonstrates that the
16 88.5 million coming from the forecast analysis is reasonable
17 and conservative.

18 **Q.** So are the amounts that we're looking at here in this
19 \$80 million or higher range -- are they impactful to Ariosa's
20 business? Were they impactful to Ariosa's business at that
21 time?

22 **A.** Yes. And here is an excerpt from the amended S-1 filing
23 providing some financial information on Ariosa.

24 You'll see the first three columns of data are for the
25 years 2011, 2012, and 2013.

1 The next two columns are for the first quarter of 2013.

2 And the last one is the first quarter of 2014.

3 There's two interesting observations here.

4 The first is that the operating expenses for Ariosa during
5 this time period were quite significant.

6 For example, in 2013, the annual expenses were about
7 \$37.7 million.

8 The other interesting point is on the bottom line here,
9 the net income. And you can see in each year there was
10 negative income to Ariosa. They were operating at a loss. And
11 that changed at the first quarter of 2014, just prior to the
12 IPO.

13 Now, the magnitude of the profit there is small for
14 Ariosa. But at least it was turning positive at that point.

15 **Q.** Did you consider the Roche acquisition?

16 **A.** Yes, I analyzed the Roche acquisition.

17 **Q.** And what did you conclude, or how did that impact your
18 findings?

19 **A.** Well, there's a couple of interesting points there.

20 So the value of Ariosa that I was showing you -- the
21 outstanding common stock is about \$281 million; and then they
22 were going to raise, on top of that, approximately 52 to
23 \$60 million, as well.

24 Later in time, they were acquired by Roche for
25 \$400 million, which at first blush one might think indicates

1 that there is no harm, and all is well and good. But it's
2 really -- that comparison would be apples and oranges, because
3 of two factors. One is that across that time period, the value
4 of companies in this space went up about 39.5 percent. So
5 there was a nearly 40 percent increase in value during that
6 time period, so there was a time change. The second point is
7 that when Roche acquired Ariosa, they benefited from the
8 control of the company, and they paid a control premium, which
9 is common.

10 Case in point is Verinata. When Verinata was acquired by
11 Illumina, just prior to the acquisition their value was
12 \$128 million.

13 In contrast, Illumina purchased them for \$350 million.

14 So that difference is the control premium. It's not
15 reflecting the underlying financial performance of the company,
16 which is what -- where the harm occurs.

17 **Q.** Did Ariosa's eventual acquisition by Roche eliminate the
18 harm to Ariosa that was caused by Illumina's conduct?

19 **A.** No, it did not.

20 The funds that were paid by Roche to Ariosa did not go to
21 Ariosa, the company; it went to Ariosa the shareholders.

22 So there was no additional capital infusion into Ariosa
23 that would then provide the benefits that the IPO would
24 provide, such as sales growth, marketing growth, R & D. And it
25 also is something that doesn't allow the other benefits of an

1 IPO: Better name recognition; auditing, which provides better
2 terms with vendors. There's a lot of other benefits that come
3 from an IPO beyond just the capital infusion.

4 Q. So taking together all of those different methods you took
5 to look at the issue of harm, what is your ultimate take-away
6 regarding Ariosa's counterclaim damages?

7 A. In my view the harm to Ariosa was substantial. And I have
8 calculated that a reasonable and conservative estimate is
9 \$88.5 million.

10 Q. How confident are you that the harm to Ariosa exceeds the
11 \$14 million we heard Ms. Yee talk about earlier?

12 A. Extremely confident.

13 Q. Well, let's turn now to the plaintiffs' claim.

14 Did you also analyze the opinions that were presented by
15 the plaintiffs' expert regarding the patent issues?

16 A. Yes, I did.

17 Q. Could you summarize for us what your conclusions were?

18 A. Sure. So first off, the -- there's no proof of lost
19 profits; and, thus, lost profits are not the appropriate remedy
20 for calculating damages.

21 But instead, in the event you find that there is
22 infringement, and that their patents are valid, the right way
23 to measure damages is through a reasonable royalty.

24 I calculated and determined that for the '430 patent,
25 which only applies to Version 1 of Harmony™, that the

1 reasonable royalty is \$1,304,238.

2 For the '794 patent and Version 1, I determined a
3 reasonable royalty is \$1,044,494.

4 For Version 2 under the '794 patent, I determined a
5 reasonable royalty to be \$1,006,551.

6 And the total across all versions and all patents is
7 \$3,355,283.

8 Q. And just to clarify your role here, do you actually have
9 any reason to believe that there is infringement in this case?

10 A. No.

11 Q. And your task, in other words, is to present an
12 alternative just in case the jury comes to a conclusion in that
13 regard?

14 A. That's right. I had simply assumed that the patents are
15 valid and infringed, and thus calculated damages accordingly.

16 Of course, if you find that there was not infringement, or
17 that the patents are invalid, then there would be no damages.

18 Q. And is that the standard practice in patent infringement
19 cases, that both sides, no matter how vigorously they dispute
20 infringement, both sides will put on an expert for the jury?

21 A. Yes.

22 Q. Now, let's just briefly do a little bit of background on
23 the prenatal testing market that informed your opinions.

24 Can you walk us through what we're looking at here?

25 A. Sure. So this is a chart that I prepared that shows the

1 growth of NIPT tests within the screening -- the prenatal
2 screening marketplace.

3 So prior to NIPT, there were approximately 2.8 million
4 prenatal screening tests being performed in the United States
5 each year. And what you can see is this is showing it on an
6 annual basis from 2012 to 2016.

7 In 2012, we had the initial entrants supplying NIPT tests,
8 and then additional entrants coming in thereafter.

9 So what this is really showing is that over time, as the
10 providers are generating acceptance and awareness for the
11 tests, they're getting greater penetration into the screening
12 marketplace.

13 You know, the acceptance comes from clinical research,
14 publications, and proof that the tests are reliable. The
15 acceptance comes from efforts that are undertaken by Ariosa, as
16 well as others, to educate and inform the community. So this
17 is getting out there and talking to physicians and physician
18 groups, and hospitals, and payers, and insurance providers, and
19 doing what they can to really try to educate the marketplace as
20 best as they can.

21 And you can see that the growth has been significant. Yet
22 even as of 2016, still 68 percent of patients who are opting to
23 get screened -- they're still only getting the traditional
24 screening and not an invasive -- non-invasive prenatal test.

25 **Q.** And turning to your next slide.

1 What are we looking at here? And how does this relate to
2 the market dynamic?

3 **A.** So this is a chart I put together to try to kind of help
4 explain why we're seeing the growth that we're seeing, and why
5 it didn't just change overnight to everybody starting to
6 purchase the test.

7 So on the left-hand side we have providers, such as
8 Ariosa, and distributors. So the providers and the
9 distributors have been seeking to get their test to patients,
10 to pregnant women. And there's a number of factors that impact
11 whether or not they're able to connect with that patient.

12 You know, first and foremost is geographic location.
13 Sometimes we think of this just as U.S. versus international.
14 But when you think about the international landscape, it's a
15 very fragmented marketplace.

16 When you look over in Europe, there are many different
17 countries, each with their different regulations. And there
18 are tests being performed by Ariosa throughout the world:
19 South America, Africa, Asia. And then even within the
20 United States, there's a big geographic mix between
21 metropolitan areas, such as San Francisco versus very rural
22 areas, east versus west.

23 And these different providers and distributors have
24 different connectivity and access to different geographies.

25 **Q.** With that background in mind, let's turn to the

1 plaintiffs' claim for lost profits.

2 I have the *Panduit* test up on the screen. Why is this
3 *Panduit* test significant to this case?

4 **A.** Plaintiffs' expert and plaintiffs' damages rest entirely
5 on the *Panduit* test. And the *Panduit* factors here -- these
6 prongs (indicating) -- have not been proven.

7 **Q.** And let's walk through that.

8 First, why do you say no patent-specific analysis

9 **A.** For two reasons. First off, the plaintiffs have not put
10 forth an analysis of lost profits that would be specific to
11 each patent. They have just lumped everything together.

12 Secondly, they have not performed an analysis separate for
13 Verinata versus Illumina, even though those are still separate
14 entities, as reflected as being different parties in this
15 litigation.

16 **Q.** And let's touch briefly on your second bullet point about
17 non-infringing alternatives.

18 **A.** As we've heard for the '430 patent, Version 2 is
19 noninfringing. And the microarrays that that's based upon were
20 available prior to, you know, the launch of Harmony™.

21 And for the '794 patent, there's the Agilent SureSelect
22 approach, and that, too, was available well before Harmony™
23 launched.

24 So there were these alternatives that would have been
25 available to Ariosa had they proceeded and been confronted with

1 the infringement.

2 **Q.** And what about the dozens of different NIPT products on
3 the market? Have you see any evidence from the plaintiffs that
4 any of those alternatives infringe either patent in this case?

5 **A.** No, I have not seen any evidence of that.

6 **Q.** Let's dig into your third bullet point about the Market
7 Approach being -- in your words -- fundamentally flawed.

8 Can you elaborate on that?

9 **A.** Yes. So going back to this slide that I showed you
10 earlier, the fundamental flaw is that plaintiffs assume that
11 all of the NIPT sales in that sales growth -- all of that would
12 have occurred exactly the same had Ariosa not been in the
13 marketplace.

14 And thus, he's assuming that all of the sales -- each and
15 every one of the tests that were provided by Ariosa -- would
16 have been made by another provider. And that's just false.

17 **Q.** Has there been any testimony in this trial that confirms
18 and further validates your conclusion that plaintiffs' expert's
19 assumption is incorrect about the economics of this market?

20 **A.** Yes. There's been a variety of the testimony explaining
21 how this marketplace has evolved over time from Mr. Bird and
22 Mr. Rava.

23 In particular, I found Dr. Rava's testimony to be quite
24 interesting. He explained that there's a benefit to all of the
25 market participants, including Verinata; that there's a benefit

1 to having Ariosa in the marketplace, because it helps generate
2 awareness and acceptance.

3 And, you know, naturally, there's also some competitive
4 aspects to the relationship, too. So there's a tradeoff that's
5 occurring. However, he explained that there's not a way to be
6 able to measure, you know, that tradeoff, and whether it's on
7 net a benefit, or -- or not.

8 **Q.** Is it possible to reconcile Mr. Malackowski's 100 percent
9 assumption with Dr. Rava's testimony?

10 **A.** No, they're directly at odds.

11 **Q.** And can you give an example of some of the areas of tests,
12 understanding it's not your burden to show an absence of lost
13 profits; but can you give an example of some of Ariosa's tests
14 that certainly did not result in lost profits for either of the
15 plaintiffs?

16 **A.** Yes. 17.6 percent of the tests -- or roughly 148,000 of
17 the Ariosa tests -- were provided without any fee or any
18 payment. And there are two problems with that.

19 First, if, instead, those tests were to be provided at a
20 higher price -- \$100, \$200, \$400 -- fewer of those tests would
21 have been purchased. It's fundamental aspect of law of demand.
22 And this marketplace is not immune from that law, as well.

23 Secondly, had, instead, those providers priced it at zero,
24 then they would not have been losing profits; but, rather, that
25 would have been a negative; that would have been a loss or an

1 additional loss that they would have incurred.

2 **Q.** Let's turn to the 40 percent of sales that were in the ex
3 U.S., the international markets.

4 Well, I guess why don't you walk us through this slide
5 DX 617.

6 What are we looking at here?

7 **A.** So this is explaining -- just to start off, about 265,000
8 of the tests are being performed outside the U.S. And we've
9 heard testimony along the lines that Ariosa has been present in
10 roughly 100 countries.

11 Well, here, this is a document from December 2014 showing
12 all of the different countries that Ariosa is in. And while it
13 may seem intuitive that they would be in, say, a lot of the
14 European countries, there's also a lot of other countries that
15 might not be as intuitive, whether it be Angola or Kenya or
16 Ethiopia; and they really did start to penetrate the entire
17 global landscape.

18 **Q.** Have the plaintiffs presented any evidence that either
19 they or companies they referred to as partners would have made
20 sales in any of these countries?

21 **A.** No. There simply is no evidence that Verinata would have
22 been in these countries and making these sales.

23 And there's certainly no evidence for Illumina's
24 customers.

25 **Q.** Did Illumina actually present any evidence of the sales or

1 manufacturing capabilities of any of its partners?

2 **A.** No, none.

3 **Q.** Could you elaborate a little bit more on the absence of
4 economic evidence as to whether any of these third parties lost
5 sales to Ariosa; and, if so, how much?

6 **A.** So the various factors that are at issue for evaluating
7 whether or not Verinata lost profits are the very same factors
8 that are at issue in evaluating Illumina's partners or their
9 customers: To see if they would have lost sales and lost
10 profits.

11 We have zero information on these other entities. We
12 don't know how they would be able to address each of the unique
13 patients that are out there. We don't know their geographic
14 reach. We don't know their distributorship. We don't know
15 what their sales force capabilities are. We don't know their
16 pricing. There's a whole host of factors that we don't know.

17 **Q.** And do we know whether they're large or small, for
18 example?

19 **A.** No, we do not. You know, and, in fact, there are a number
20 of, you know, international entities; there's companies such as
21 BGI and Promethea, and they're operating in many, many
22 different countries throughout the world; and they do not use
23 Illumina's platform. And so if they're making even, you know,
24 some of those sales, then there would not be any sort of lost
25 profits.

1 And to be clear, all of this is just premised upon Ariosa
2 not existing, not being in the marketplace. But we know that
3 because of the alternatives that were available to them, they
4 would have remained in the marketplace.

5 Q. So can you summarize for us your ultimate conclusion about
6 whether plaintiffs are entitled to lost profits under the
7 *Panduit* test?

8 A. Yes. Quite simply, is that plaintiffs have not proven the
9 *Panduit* test has been met; and they have not proven that lost
10 profits are appropriate.

11 Q. Does this mean that if the plaintiffs prevail in any of
12 the patent issues, that they can't recover any damages?

13 A. No. So in the event there is a finding of infringement
14 and invalidity, then the appropriate way to measure damages is
15 through a reasonable royalty.

16 Q. And did you consider the same hypothetical negotiation
17 framework that we briefly heard about from the plaintiffs'
18 expert?

19 A. Yes.

20 Q. Can you explain for the jury the key economic
21 considerations for the '430 patent hypothetical negotiation?

22 A. So this negotiation would have occurred in November 2012
23 when the '430 patent issued. And at that time Ariosa would not
24 have a need for this technology, because they had the
25 alternatives available to them, importantly, the microarray.

1 On the other hand, Verinata had demonstrated that they did
2 not intend to use the '430 patent. There was not any
3 indication that there would be anybody who would be using the
4 '430 patent. So this would give them an opportunity to
5 actually earn some income from that patent that they otherwise
6 wouldn't get.

7 Moreover, as I described earlier, Verinata would recognize
8 that while there are some competitive aspects to the
9 relationship between Ariosa and Verinata, there's also a very
10 tangible benefit to having Ariosa in the marketplace generating
11 awareness.

12 **Q.** And how about the '794 patent hypothetical negotiation?

13 **A.** Well, here, again, Ariosa would not have a need for the
14 '794 patent, because there's an alternative in the SureSelect
15 platform.

16 And in addition, Illumina would have multiple motivations
17 for entering into an agreement.

18 First off, they were an investor in Ariosa.

19 And second of all, they were a supplier to Ariosa.

20 And keep in mind that the hypothetical negotiation is in
21 March 2012, when Ariosa began its commercial sales of the
22 Harmony™ product. And this is just after the time that
23 Illumina and Ariosa had entered into the Sale and Supply
24 Agreement, which is, you know, further evidence of their
25 cooperation at that point in time.

1 Q. Now, do you agree with the plaintiffs' expert's
2 conclusions regarding what the outcome would be of this
3 hypothetical negotiation?

4 A. No, I do not.

5 Q. Can you highlight for us the key problems with the
6 plaintiffs' expert's analysis?

7 A. At a high level, he has chosen the wrong agreements to use
8 as benchmarks. He has then inflated the royalty rates from
9 those benchmarks.

10 And he has not recognized apportionment, which would
11 account for the economic contributions of the asserted
12 technology.

13 Q. Now, with the chart we have on the screen, 6.24, can you
14 elaborate on your observation that the plaintiffs' expert's
15 started with the wrong agreements?

16 A. Yes. So these are the agreements that were considered
17 both by myself and plaintiffs' expert.

18 And what I have put up here is for each of these
19 agreements, I've put up the range of rates that are specified
20 in those agreements.

21 For example, at the far left you'll see the agreement
22 between the University of Louisville and Ariosa; and that has
23 royalty rates that range from one percent to three percent.
24 There's a list rate of three percent, and then there are
25 reductions down to one percent, which I'll explain a little bit

1 later.

2 But what you see is that rather than choosing any of the
3 agreements from Ariosa or Verinata, who are parties to the
4 hypothetical negotiation, he chose agreements with Sequenom;
5 and those happen coincidentally, perhaps, to have a rate that's
6 at the highest end of the range.

7 **Q.** You also stated that the plaintiffs' expert inflated the
8 royalty rate.

9 Can you explain what you meant by that?

10 **A.** Yes. So he uses the highest rates from the agreements
11 that have the highest rates. He then adds those together, even
12 though the underlying agreements reflect that there should be
13 an adjustment that should be made if they're going to be added.

14 And then he takes a further step, and rather than applying
15 the royalty rates to Net Sales, as all of these agreements
16 have, he applies it to a different amount, which inflates the
17 rate in total to about 24 percent.

18 **Q.** What was the different amount that he applied it to?

19 **A.** So he used what he called a projected amount of \$761,
20 which is not the amount that was being received by Ariosa. And
21 it's far more than what others were receiving in the
22 marketplace, including Verinata.

23 **Q.** So we had a little bit of discussion with the plaintiffs'
24 expert about how you would actually calculate out the effective
25 rate based on that \$761 figure.

1 Could you walk us through the math on that?

2 **A.** Certainly.

3 So for the '430 patent, they had put forth a royalty of
4 \$45.50 per test.

5 And there are two ways that one can get there. One can
6 take the six percent multiplied by the \$761 figure that they
7 had put forth. Or you can calculate the same amount by
8 applying a rate of 12 and a half percent to the actual sales
9 amount of \$365.

10 So we can do the same thing for the '794 patent; and we
11 can just see that \$38 can be calculated in either of two ways.
12 And thus, if you apply it to the rate to the actual selling
13 price -- average selling price -- for the '794 patent, then you
14 see that it's a much higher amount of 11.7 percent.

15 **Q.** And cumulatively, what are the rates together that
16 Mr. Malackowski used?

17 **A.** Ultimately, it adds up to about 24 percent.

18 **Q.** And how does that effective 24 percent of Net Sales
19 rate -- how does that compare to all of the licensing
20 agreements that you reviewed throughout the industry that
21 predated the hypothetical negotiation?

22 **A.** It is way out there, as an outlier. You can see it
23 visually in this chart, where it is four times the amount of
24 any other agreement at the high rate, and much more than
25 anything else.

1 We can also see that there is simply, from the financial
2 data in the S-1, simply no way that Ariosa would be able to pay
3 this type of a royalty; and simply no way that they would be
4 agreeable to it.

5 **Q.** What is the economic evidence about whether Ariosa,
6 Verinata, or Illumina expected Ariosa's net revenues to be
7 somewhere at this level Mr. Malackowski used at the time of the
8 hypothetical negotiation?

9 **A.** Well, for Verinata, the hypothetical negotiation is around
10 Thanksgiving in 2012; and at that point in time there had
11 already been a number of months of actual sales both for
12 Verinata as well as for Ariosa.

13 And one can look at it. We had -- you know, the data for
14 Ariosa are roughly what I just showed you for that time period.
15 And for Verinata they were just a little bit higher. So we
16 already had that actual data versus this projection.

17 For Illumina, they were an investor in Ariosa; and the
18 information that they invested in was that the sales price that
19 was sought was going to be about \$250 for the Ariosa test.

20 **Q.** Let's turn to your third category of critique, which is
21 the lack of apportionment.

22 Do any of the NIPT licenses that you reviewed contain
23 mechanisms for apportioning or otherwise accounting for the
24 fact that multiple different technologies are contributing to a
25 product?

1 A. Yes. All of these agreements, except for one, have
2 mechanisms to reduce the royalty to account for other
3 technologies.

4 So if other technologies are being incorporated, then --
5 and being paid for, then those rates would be reduced. The one
6 exception is the Boston University agreement that already had a
7 lower rate of .7 percent. But all of the other ones have these
8 reductions.

9 Q. Let me pull this slide back up.

10 (Document displayed.)

11 THE WITNESS: So you can see the B.U. agreement there
12 in yellow. It's the B.U. Sequenom agreement at the .7 percent
13 royalty.

14 But if we go back to the other slide that lists the
15 discounts, here you'll see that the amount that the rates would
16 be discounted is significant, and it's in each and every
17 agreement.

18 The University of Louisville agreement had the rate
19 dropping from three percent down to as much as one percent,
20 which is a 67 percent drop. And the other agreements have
21 between 67 percent down to 50, or a 30 percent reduction.

22 And this is important, because not only for the fact of
23 there being an actual reduction of royalty payments in these
24 agreements, but it reflects the acknowledgment in the industry
25 and by the parties that when there are multiple technologies

1 contributing to a technology, then one reduces the royalties.

2 **BY MS. GLASSER**

3 **Q.** Well, let's walk through the calculation that you did
4 based upon your comparable license analysis.

5 What are we looking at here?

6 **A.** So I determined that the three most comparable benchmarks
7 here are the University of Louisville/Ariosia agreement, the
8 Massachusetts/Verinata agreement, and the Stanford/Verinata
9 agreement.

10 As you heard from Dr. Quackenbush, he explained that the
11 technologies in each of these agreements are technologically
12 comparable to the '430 and '794 patents; and similarly, I
13 determined that they are economically comparable to the
14 hypothetical negotiations. However, there are several
15 adjustments that do need to be made.

16 **Q.** How, if at all, does the fact that these -- two of these
17 three anyway, are with universities? How does that impact the
18 analysis?

19 **A.** It does not impact the analysis, because universities are
20 seeking to maximize their revenue and their income, just like a
21 corporation is seeking to do.

22 I've had the opportunity to work with, you know, M.I.T.,
23 Harvard, Columbia, University of Pennsylvania, and they all are
24 seeking to maximize the returns on their IP as best as they
25 can.

1 Q. Just like for-profit businesses do?

2 A. Absolutely.

3 Q. Now, what did you do to adjust for any differences between
4 the agreements you focused on and the hypothetical negotiation?

5 A. So there are four key differences between these agreements
6 and the hypothetical negotiations.

7 The first is that each of the agreements is for exclusive
8 rights to the patents; whereas, at the hypothetical negotiation
9 it would be for a nonexclusive right. And here that would
10 cause the royalties to be even lower than otherwise would be
11 the case, because exclusivity can confer additional benefits.

12 In addition, each of the agreements provides for
13 sublicensing rights; and sublicensing would allow, then, Ariosa
14 or Verinata, for example, then to go license the technology to
15 somebody else, which also is of value.

16 And so the hypothetical negotiation does not have that, so
17 we need to reduce the rates.

18 The hypothetical negotiations -- each one is for a single
19 patent; whereas these agreements are for a collection of
20 technologies.

21 And furthermore, one needs to account for the economic
22 contributions of the '430 and '794 on the one hand, relative to
23 the contributions that are in these agreements, and that Ariosa
24 is actually generating.

25 Q. And as the result of --

1 Actually, I should ask you. Are you familiar with the
2 *Georgia Pacific* factors?

3 **A.** Yes.

4 **Q.** And how does what you were just describing relate to those
5 factors?

6 **A.** It directly relates to the *Georgia Pacific* factors. I
7 have considered all 15 of those. These are the key issues
8 that -- for these agreements -- require adjustment.

9 And the end result is that I determined that the
10 appropriate rate royalty rate for the '794 patent is
11 .75 percent.

12 For the '430 patent, I determined that the right royalty
13 rate is one percent.

14 And because I had, in my view, properly accounted for the
15 singular patents, and their relative contributions, when
16 they're added together it's 1.75 percent.

17 **Q.** Why is the '794 rate lower than the '430?

18 **A.** Well, for a couple of reasons.

19 One, is it does not provide the same degree of
20 contribution; and it is with Illumina, who at the time was an
21 investor and supplier in Ariosa.

22 **Q.** Now, how did the testimony of Mr. Flatley inform your
23 conclusion that Ariosa would not have been required to pay a
24 heavy toll by Illumina back at the time of the hypothetical
25 negotiation?

1 **A.** Well, Mr. Flatley explained that Illumina was an investor
2 in Ariosa; and he had even sent out an e-mail to his team to
3 make sure that Ariosa was well taken care of, because they were
4 an investor of Illumina.

5 **Q.** Now, some of the agreements include an equity interest or
6 other upfront payments.

7 Did that require any upward or downward adjustment to your
8 rate?

9 **A.** No, it did not.

10 So some of these agreements have, you know, equity
11 payments or other upfront milestone-type payments. But those
12 are separated in time.

13 So keep in mind when these agreements are entered into,
14 these are all prior to the launch of Harmony™, or verifi®, as
15 the case may be.

16 And so the patent holder wants to have consideration or
17 payment for the period of time from when they entered the
18 agreement before the product actually gets launched
19 commercially. Then once the product is launched commercially,
20 that's when the royalties kick in.

21 And we, at the hypothetical negotiation, are at the point
22 right prior to the commercial launch. And so what's applicable
23 for that period of time, and for our damages analysis, is the
24 running of royalties that are specified in the agreements as
25 properly adjusted.

1 Q. Could you recap for us, Dr. Sullivan, what is your
2 ultimate conclusion only in the event, of course, that the jury
3 were to find any liability on the part of Ariosa?

4 A. So, again, I've determined that lost profits have not been
5 proven, and that lost profits are not the appropriate damages
6 remedy; but, instead, once you look at a reasonable royalty,
7 and the total amount across both patents and all versions of
8 Harmony™ is \$3,355,283.

9 MS. GLASSER: Thank you very much, Dr. Sullivan.

10 And I'm sorry you're going to have to sit up there for
11 just a moment. We have some housekeeping to admit some of the
12 documents that you relied upon.

13 And the parties, Your Honor, have agreed, similar to what
14 we did with Mr. Malackowski, that we could admit them full
15 scale.

16 MR. COX: Correct, Your Honor.

17 THE COURT: Okay.

18 MS. GLASSER: The exhibits to be admitted are 1059,
19 1087, 1102, 1133, 1160, 1226, 1252, 1318, 1362, 1385, 1414,
20 1587, 1589, 1590, 1591, 1594, 1608, 1615, 1648, 1649, 1650,
21 1651, and one more, or no?

22 MR. GINDLER: I think you mentioned two pages on
23 1396.

24 MS. GLASSER: Okay. Oh, sure. So there's been --
25 the S-1 has been admitted, but there was discussion of which

1 pages to admit.

2 MR. GINDLER: It's the amended S-1.

3 MS. GLASSER: Right. So this is 1396, pages 11, 12,
4 40, and 41.

5 THE CLERK: 1396, 11, 12, pages --

6 MS. GLASSER: 11, 12, 40 and 41.

7 THE CLERK: 40 and 41. Thank you.

8 THE COURT: Thank you.

9 MS. GLASSER: Thank you.

10 (Trial Exhibits 1059, 1087, 1102, 1133, 1160, 1226, 1252,
11 1318, 1362, 1385, 1414, 1587, 1589, 1590, 1591, 1594, 1608,
12 1615, 1648, 1649, 1650, 1651, 1396-11, 1396-12, 1396-40, and
13 1396-41 received in evidence)

14 MS. GLASSER: Pass the witness.

15 THE CLERK: And 1396, you say, was on your list?

16 MR. GINDLER: It was admitted.

17 THE CLERK: It was previously admitted. It's not on
18 this list?

19 MR. GINDLER: That's correct.

20 THE CLERK: Good. I want to make sure. Thank you.

21 THE COURT: Mr. Cox, is this you?

22 MR. COX: It's me.

23 THE COURT: Okay.

24 MR. COX: Thank you, Your Honor.

25 (Whereupon a document was tendered to the Court.)

CROSS-EXAMINATION

BY MR. COX

Q. Good afternoon, Mr. Sullivan?

A. Good afternoon.

Q. I have a few questions to follow up on your testimony.

A. Thank you.

Q. The first one, Mr. Sullivan: Were you here during opening when Mr. Gindler gave his opening statement?

A. No. But I did read the transcript.

Q. Okay. And so you read Mr. Gindler's statement in his opening that all we want is we want our money back; we spent 17 and a half million dollars on Illumina's equipment and supplies over the years, only to have it rendered worthless. We'd like our money back.

Did you read that?

A. That sounds familiar.

Q. And in the opinion you've just provided to the jury, you did not simply ask that the jury give Ariosa its money back for the equipment and supplies it purchased from Illumina; right?

A. I'm not asking the jury to give any money to anyone; but, rather, I was asked to calculate the harm, and that's what I did.

Q. So let me get it right, on the harm that you testified about is there's basically four categories of harm; right? Which was harm from cancellation of the IPO, harm from sunk

1 costs of the -- of the IPO, difficulty securing distribution
2 partners, and acceleration of Ariosa's transition to the
3 microarray platform; right? Those are the four categories?

4 **A.** Those are the ones that I addressed, yes.

5 **Q.** Now, with regard to difficulty securing business partners,
6 you actually didn't see any evidence from potential partners
7 like Quest or LabCorp testifying that they didn't go forward in
8 a relationship with Ariosa because of the lawsuit that you
9 claim is the basis for the harm; right?

10 **A.** I have seen documents, but I do not recall testimony.

11 **Q.** Okay. You didn't, when counsel was asking you questions,
12 you didn't identify a single document to support your opinion
13 that there was some harm based upon a failure to secure
14 business partners; is that correct?

15 **A.** I could not say for sure what were in all the exhibits
16 that were just read in. Certainly my report --

17 **Q.** That's not my question, sir.

18 **A.** -- would have that in there.

19 **MS. GLASSER:** Excuse me, Your Honor. Counsel is
20 interrupting the witness.

21 **THE COURT:** Don't interrupt him.

22 Also, just listen to his question and answer exactly what
23 he asks you, okay?

24 **THE WITNESS:** I will do my best.
25

1 BY MR. COX

2 Q. The question, sir, was during the testimony you just gave
3 a few moments ago, you didn't identify a single document or any
4 testimony to support your opinion that there was some lost
5 business opportunities because -- specifically because of the
6 lawsuit?

7 A. Ah, I would have to disagree with that.

8 Q. Okay. Let's talk about the difficulty raising revenue by
9 loan, by securing loans.

10 You testified that Ariosa would be incapable of securing
11 the financing for 50 to \$60 million that it lost from the
12 failed IPO; right?

13 A. As a result of the lawsuit, and the breach of contract,
14 and breach of covenant.

15 Q. Now, you haven't testified about any process by which
16 Ariosa attempted to get the 50 to \$60 million in loans and was
17 denied; right?

18 A. That's right.

19 Q. So let's talk a little bit about the damages.

20 Now, you just mentioned that the damages are based on an
21 alleged breach of contract and breach of the good faith and
22 fair dealing covenant; right?

23 A. That's right.

24 Q. Now, those are based -- the breaches you're talking about
25 are breaches of the Sale and Supply Agreement between Ariosa

1 and Illumina; right?

2 **A.** That is my understanding.

3 **Q.** Now, in none of your testimony right now did you even
4 refer to the Sale and Supply Agreement; right?

5 **A.** Actually, I did.

6 **Q.** Okay. Well, let's talk about the portions of the Sale and
7 Supply Agreement that actually bear upon the damages.

8 Can we call up Exhibit 16, page 11, please? And
9 specifically paragraph number 18.

10 (Document displayed.)

11 **BY MR. COX**

12 **Q.** You'll see that there is this limitation of liability
13 provision in the Sale and Supply Agreement.

14 Do you see that?

15 **A.** I see it, yes.

16 **Q.** And your testimony in your report you never mention this
17 limitation of liability; right?

18 **A.** That's right. That would be a liability issue, and not a
19 damages issue.

20 **Q.** Okay. Now, let's talk about that.

21 So under the limitation of liability, it says:

22 "In no event shall Illumina or its supplier or
23 customer be liable to each other or any third party
24 for costs of procurement of substitute products or
25 services, lost profits, data or business, or any

1 indirect, special, incidental, exemplary,
2 consequential, or punitive damages of any kind
3 arising out of or in connection with this agreement."

4 Do you see that?

5 **A.** I can see that, yes.

6 **Q.** You never addressed in your report or in your direct
7 examination how the damages you're seeking fit within the scope
8 of allowable damages under the Sale and Supply Agreement;
9 correct?

10 **A.** I am not an attorney, and, thus, that would be outside the
11 scope of my work.

12 **Q.** Right. So you just didn't address it?

13 **A.** That's true.

14 **Q.** Okay. Now, even if Ariosa could prove that it had a right
15 to some damages, under the limitation of liability, those
16 damages are capped; right?

17 **MS. GLASSER:** I'm going to object. And it might be
18 helpful to note that the parties are submitting jury
19 instructions on this. And the jury will get some guidance from
20 the Court ultimately about the legal issues.

21 **MR. COX:** Your Honor, I don't know why that's an
22 objection.

23 **THE COURT:** It's a legal question, and you can't
24 answer it. That's the objection.

25 **MR. COX:** I'm just going to read the portion of the

1 limitation liability and see if he can --

2 **THE COURT:** You already read it, I thought.

3 **MR. COX:** No, I have another part, Your Honor.

4 **THE COURT:** Well, then you're asking him what does
5 that mean?

6 **MR. COX:** No, I'm not asking what it means.

7 **THE COURT:** What are you asking him?

8 **MR. COX:** I'm asking him if he considered it.

9 **THE COURT:** Okay.

10 **MS. GLASSER:** Then I object. Asked and answered.
11 That was answered already.

12 **THE COURT:** Well, he's going to do the other half, he
13 says.

14 **MS. GLASSER:** Okay.

15 **MR. COX:** Thank you.

16 And Mr. Bonini, can you highlight the sentence that says:
17 "Illumina's total and cumulative liability arising
18 under or in connection with this agreement, whether
19 in contract, tort, including negligence, strict
20 liability, or otherwise, shall in no event exceed the
21 amount received by Illumina from customer -- that's
22 Ariosa -- under this agreement."

23 Do you see that?

24 **A.** I do.

25 **Q.** Did you consider that in forming your opinions?

1 A. I have considered that more recently, as it's been
2 presented, and I've seen it. Yet it did not factor into my
3 analysis or my report, because this really is a liability
4 issue, and there's some factual dispute --

5 Q. That's --

6 A. -- over the applicability of that.

7 Q. That's not my question.

8 A. So I addressed the calculation of the harm separate and
9 apart from the liability issue.

10 Q. Okay. So in forming your opinions, you didn't rely upon
11 limitation of liability which caps Ariosa's damages at the
12 \$14 million figure that Ms. Yee just testified to; right?

13 MS. GLASSER: Objection. Calls for a legal
14 conclusion.

15 THE COURT: He didn't consider the paragraph; he's
16 just told you that. And now you're testifying about what the
17 consequence would be.

18 MR. COX: Actually, Your Honor, he actually said he
19 did consider it. So recently he considered it.

20 THE COURT: Recently. But he said for purposes of
21 his report, he didn't take it into account.

22 MR. COX: Okay.

23 THE COURT: I think. Isn't that what you said?

24 THE WITNESS: Yes.
25

1 BY MR. COX

2 Q. So in forming your opinions, you reviewed no documents to
3 determine how much Ariosa actually paid for equipment and
4 supplies under the agreement until the agreement expired in
5 2015; right?

6 A. I have seen some documents relating to some of the amounts
7 that were paid.

8 Q. Okay. Well, you offered no opinion regarding how much
9 Ariosa paid for equipment and supplies under the agreement;
10 right?

11 A. I have not sought to calculate that number.

12 Q. You have offered no opinion on whether Ariosa was unable
13 to use any sequencers or reagents that were supplied under the
14 Supply Agreement; right?

15 A. I'm sorry. I did not follow that.

16 Q. You have offered no opinion regarding whether Ariosa was
17 unable to use any of the equipment and supplies that were
18 supplied under the Supply Agreement; is that correct?

19 A. I have -- the short answer is that's right, I have not
20 investigated that.

21 Q. And you sat here for Ms. Yee's testimony this afternoon?

22 A. Right before mine, yes, indeed.

23 Q. And do you have any reason to believe that Ariosa did not
24 actually use all of the reagents that were supplied under the
25 Supply Agreement?

1 A. I don't have a basis. I could conjecture that there would
2 be some shrinkage or loss or un-usage or --

3 Q. Conjecture is not helpful to anybody.

4 A. Or what have you. But I don't --

5 THE COURT: Don't conjecture.

6 BY MR. COX

7 Q. Conjecture is not helpful to anybody.

8 You have no reason to believe that they didn't use the
9 supplies that were provided; right?

10 A. Well, I can conjecture reasons, but I can't confirm it one
11 way or the other.

12 Q. Okay. So you also have no opinion regarding whether any
13 of the sequencers that Illumina supplied to Ariosa didn't work
14 as intended; right?

15 A. I have not investigated that issue.

16 Q. Okay. And you haven't offered any opinions regarding
17 whether any of the equipment or supplies that were supplied by
18 Illumina to Ariosa were not fit for the purpose that they were
19 supplied; right?

20 A. I have not sought to make that determination one way or
21 the other. That would be well outside the scope of my work.

22 Q. Right. So as far as you know, you have no reason to doubt
23 that as far as the equipment and supplies supplied under the
24 agreement, Illumina supplied all the supplies, and Ariosa used
25 those supplies until the agreement expired in 2015; right?

1 **A.** Oh, I disagree, because the agreement provided, as I
2 understand it, a license to the '794 patent, according to
3 Ariosa.

4 And because we're sitting here today, that's because --

5 **MR. COX:** Your Honor, can we -- we don't have much
6 time.

7 **THE WITNESS:** -- the benefits of that license was not
8 afforded to Ariosa.

9 **MR. COX:** It's not responsive.

10 **THE COURT:** Overruled. It can stand.

11 **BY MR. COX**

12 **Q.** Okay. Now you're talking about infringement.

13 You're not a technical expert; right?

14 **A.** Not in the technical fields, here. My fields are
15 economics, finance, and statistics.

16 **Q.** Right. And you have no opinion as to whether or not
17 Ariosa infringes the '794 patent or not; right?

18 **A.** That's right, I have no opinion on that.

19 **Q.** You have no opinion whether they infringed the '430 patent
20 or not; right?

21 **A.** That, too, is right.

22 **Q.** Right. So your job as a damages expert is to assume that
23 there is infringement, and the patents are valid; right?

24 **A.** I have made that assumption, yes.

25 **Q.** Okay. So let's talk a little bit about the IPO.

1 You opined that Ariosa's inability to move forward with
2 its IPO resulted in a loss of company value; right?

3 **A.** It caused a loss of company value which reflects the
4 harmed financial performance.

5 As I indicated, I used the company value as a means to
6 measure the impact of -- on the financial performance.

7 **MR. COX:** Mr. Bonini, can you pull up the trial
8 transcript at page 881, lines 14 to 21, please?

9 (Document displayed.)

10 **BY MR. COX**

11 **Q.** Were you here for the testimony of Mr. Stuelpnagel,
12 Mr. Sullivan?

13 **A.** No, but I did read his transcript. Or I read the
14 testimony from the transcript.

15 **Q.** Now, Mr. Stuelpnagel was asked the following question and
16 gave the following answer:

17 "Okay. And then in terms of what the IPO would have
18 produced in terms of the price it would have been or
19 the market capitalization that it would have been,
20 that's speculative; right? That's all just
21 speculative?"

22 (As read.)

23 And the answer to that question was:

24 "Nobody knew what would happen had we been allowed to
25 go public. We obviously think we would have been

1 highly successful, but we weren't given the chance to
2 run that experiment."

3 Did you consider Dr. Stuelpnagel's testimony in offering
4 your opinion to the jury that Ariosa should receive almost
5 \$100 million in damages based on the loss of value from the
6 failure of the IPO?

7 **A.** Yes, I did give this consideration. And it makes perfect
8 sense, because looking at the IPO and the pricing, nobody can
9 predict that with absolute precision. But what we can do is we
10 can develop reliable estimates?

11 And as I indicated, during that time, 76 percent of the
12 biotech IPOs priced at or above the range that was set for
13 their pricing. And we have a great deal of evidence indicating
14 that there would be a premium on top of that to account for the
15 20 percent IPO discount.

16 Even if you ignore the IPO discount -- the 20 percent
17 effect -- you are still at a number that is well north of the
18 14 or 17 million that you've been discussing here today.

19 **Q.** So you disagree with Dr. Stuelpnagel that it would be
20 speculative to place a value on the IPO that didn't go forward,
21 because you didn't have the price, didn't have the market
22 capitalization numbers; right? You disagree with that?

23 **MS. GLASSER:** Objection. Counsel is testifying and
24 misstating Dr. Stuelpnagel's testimony.

25 **THE COURT:** Sustained.

1 **MR. COX:** Okay.

2 **Q.** Now, you would agree with me, Mr. Sullivan, that
3 speculative damages are not allowed to be awarded in a case;
4 right?

5 **A.** That's probably true.

6 **Q.** Now, you gave an opinion today that had the IPO gone
7 forward and Ariosa went through the process, that it would have
8 been worth \$281 million; is that right?

9 **A.** For the then currently outstanding shares. Then there
10 would have been the additional shares that would have been
11 issued throughout the IPO process.

12 **Q.** Okay. Now, that's an assumption, you know, based on your
13 modeling that you just described to the jury; right?

14 **A.** It's not an assumption, it's a determination of a
15 reasonably reliable estimate.

16 **Q.** Now, after the IPO, Ariosa was acquired by Roche; right?
17 You testified about that.

18 **A.** Ah, I'm sorry. Say that again. Perhaps you misspoke.

19 **Q.** I misspoke. It was my fault. I'll repeat the question.

20 After the IPO was canceled, Ariosa was purchased by Roche;
21 right?

22 **A.** Yes, that's right.

23 **Q.** And I think you referenced \$400 million; but that was
24 actually the upfront cash with milestones at about a
25 \$625 million transaction; right?

1 **A.** The initial upfront amount was 400 million, just like the
2 upfront for Verinata was 350 million.

3 And then in the event certain performance thresholds would
4 be hit thereafter in the ensuing years, there would be
5 additional payments of up to 225 million.

6 **MR. COX:** Now, can we call up slide five of
7 Mr. Sullivan's slide deck?

8 (Document displayed.)

9 **BY MR. COX**

10 **Q.** Now, under your forecast analysis, before you looked at
11 the forecast of Ariosa, and you tried to calculate damages
12 based upon, you know, a graph that you set if the forecast had
13 held true versus what actually happened; right?

14 **A.** That's not quite right, but it's along the same lines,
15 which would be slide four.

16 **Q.** Yeah. Well, I want to talk about slide five, which
17 quantifies those numbers.

18 Now, you have \$3.4 million in damages, in 2014; and then
19 34.9 in 2015; and 50.2 million in 2016.

20 Do you see that?

21 **A.** Yes, I do.

22 **Q.** Now, the acquisition by Roche was on January 12th, 2015,
23 which would be at the very beginning of where your numbers go
24 up; right?

25 **A.** Well, they would be at the beginning of 2015.

1 Q. Right. So you're -- before 2015, you have \$3.4 million in
2 damages, but after the acquisition of Roche, you have about
3 \$85 million in damages; right?

4 A. From a time period standpoint, it would be a little bit
5 different than that, but that's getting close.

6 Q. But that's after they were acquired into a much larger
7 company, where they have different forecasts and different
8 business modeling; right?

9 A. Yes. That does not change the financial performance and
10 the negative impact on the financial performance caused by the
11 canceled IPO.

12 Q. Right. But what you're looking at is not Ariosa's
13 performance as a stand-alone company during that period of
14 time. For the majority of your damages time, they were
15 actually a subsidiary of Roche; right?

16 A. Well, the financial harm --

17 Q. That's my question.

18 During the majority of the time they were a subsidiary of
19 Roche; is that right?

20 A. Well, during the majority of the time periods here, yes,
21 they were part of Roche.

22 Q. Okay. Thank you. Now, I'm trying to understand your
23 testimony about the harm.

24 So what you're saying is when Roche came in in
25 January 2015, they got a really good deal, because Ariosa

1 should have been worth more. But Roche got the company for
2 only \$625 million; and as a result of that, there's about
3 \$100 million more that Ariosa should have gotten?

4 **A.** That's not quite right.

5 **Q.** That's close?

6 **A.** No. So there's some analysis I did of the acquisition, I
7 referred to in my testimony, and we put it on an
8 apples-to-apples basis. The harm, even at the -- with the
9 Roche acquisition -- measuring the harm at that point in time
10 and looking back is still approximately 100 million.

11 **Q.** So what you're asking the jury to do is to -- is to take
12 the \$625 million Roche paid, which was admittedly a good deal,
13 and give Roche another \$100 million, so they get an even better
14 deal. That's 525 million instead of 625; right?

15 **A.** No, that's not right at all.

16 The 625 was not the total amount.

17 And we can all come up with different types of analogies.
18 I often go to vehicles and cars, because I like those.

19 And if you think about at one point in time the car gets
20 dented and dings and all beat up, that happens at the canceled
21 IPO. That harm continues regardless of whether, then, the
22 owners of that vehicle eventually get paid for the vehicle.

23 **Q.** I didn't ask about a vehicle, sir.

24 **A.** The vehicle is still harmed and damaged.

25 **Q.** You're asking the jury to give Roche another hundred

1 million dollars; isn't that right?

2 **A.** I am not making a request to the jury to make a payment.
3 I am purely calculating what the harm is.

4 And I will defer to the jury and the Court to determine
5 whether or not there's liability.

6 **Q.** Okay. So let's look at your reference to the stock price
7 that you mentioned earlier.

8 Earlier, in answer to one of my questions, you mentioned
9 that you compared Ariosa's performance to, you know, other
10 players in the market; right?

11 **A.** In what context? I've done that in a couple of different
12 ways for different analyses?

13 **Q.** Okay. So you assumed that on the first day of trading
14 Ariosa's stock price, if the IPO had gone forward, would have
15 grown at the same rate as the average of 64 other companies,
16 which is around 20 percent; right?

17 **A.** I used the other 64 biotech companies to inform that
18 estimate; but it's not based solely upon that. As I indicated,
19 there was information directly from the bankers, from JPMorgan.

20 There is a slew of empirical research that's been
21 published in academic journals on this phenomenon, and
22 quantifying it.

23 So for all of these reasons, I think 20 percent is a
24 reasonable estimate.

25 **Q.** Well, actually, wasn't JPMorgan, who was the investment

1 banker, advising Ariosa that this was a -- pardon the word --
2 crappy time to go IPO?

3 **A.** I saw some foul language being used.

4 **Q.** Yeah, that's what they were saying; right?

5 **A.** It was a bit different than that, as I recall. But I'm
6 sure we can take a look at the exact verbiage in terms of what
7 they were seeking to convey.

8 **MS. GLASSER:** I'd actually object to any further
9 questioning about this. This is about hearsay documents from
10 JPMorgan that he's not here to testify.

11 I object to counsel's characterization of these documents
12 not in evidence. It's misleading and hearsay.

13 **MR. COX:** Your Honor, it's not hearsay. He just
14 mentioned that JPMorgan was recommending this; and this is in
15 response to that.

16 **MS. GLASSER:** He said JPMorgan gave him 20 percent.
17 He didn't talk about the content of any other documents.
18 JPMorgan is not here.

19 **MR. COX:** I think the answer is in the Record,
20 anyway.

21 **THE COURT:** We'll take our recess at this time, and
22 we can discuss this.

23 Ladies and gentlemen, if you'd be ready to come back,
24 please, at 25 minutes after 2:00.

25 In the meantime, don't make up your minds or discuss this

1 matter with anybody else. You haven't heard all the evidence
2 yet.

3 (Proceedings were heard outside the presence of the jury:)

4 **THE COURT:** He says he compared 64 biotech companies,
5 and then he got information from JPMorgan. And your question
6 to him is "Didn't JPMorgan tell you this was a terrible time to
7 go forward?"

8 **MR. COX:** Right. He's suggesting that he was relying
9 on JPMorgan. And JPMorgan, we have evidence he was asked about
10 in his deposition, that JPMorgan was recommending against the
11 IPO, because it was a bad time.

12 And it goes to, you know, the next series of questions,
13 which is basically to get to his model, he looked -- he
14 included this boom time, and he didn't look at this sliver of
15 time when they were going to IPO, which was a really terrible
16 time to go to IPO.

17 **MS. GLASSER:** I have no problem with him talking
18 about what the market was like. But what he's doing is he's
19 taking the fact that at the very beginning the process,
20 absolutely everyone, including JPMorgan, was talking about how
21 you underprice an IPO. That's just a fact.

22 And what they're doing now is there's a whole slew of
23 documents produced by third party JPMorgan, most of which did
24 not go to Ariosa, all of which have serious issues with them,
25 such as --

1 **THE COURT:** Which did not go to Ariosa, what do you
2 mean?

3 **MS. GLASSER:** They're just internal JPMorgan e-mails
4 for the most part. They chose not to put in JPMorgan here, and
5 there's just a slew of evidentiary issues with them. Some of
6 them you can't tell if they were sent. They're all hearsay.

7 **THE COURT:** Did -- were they part of the materials
8 that this witness relied on?

9 **MS. GLASSER:** I think he showed some of them at the
10 deposition, or maybe Mr. Reines did.

11 But primarily the documents that he's trying to reference
12 now were not considered or relied upon by Dr. Sullivan in his
13 report. He is just trying to get them on the salacious
14 language, like the JPMorgan bankers amongst themselves using
15 salacious language. And they're not things that Dr. Sullivan
16 relied upon, and they're not in evidence. Most of them didn't
17 go to Ariosa either.

18 **THE COURT:** What is it exactly you want to do?

19 (Discussion held off the record.)

20 **MR. COX:** So I'm not trying to get salacious language
21 in, Your Honor. That's obviously not what I'm trying to do.

22 **THE COURT:** There's a lot of that going around.

23 **MR. COX:** But basically what he's saying is that
24 there was harm to Ariosa, because they didn't go forward with
25 the IPO. And at the time, the Ariosa bankers were saying it

1 doesn't matter if it's communicated to Ariosa or not, that it's
2 a crappy time for going forward with an IPO.

3 **THE COURT:** How do we know that?

4 **MR. COX:** Because we have the JPMorgan documents.

5 **THE COURT:** Well, that's hearsay; right?

6 **MS. GLASSER:** Absolutely, Your Honor. And it's not
7 in evidence.

8 **THE COURT:** It's not what he used to prepare his
9 report. If it were, I thought that's what we were talking
10 about. But if this is just other miscellaneous JPMorgan stuff
11 you've found, that doesn't come in.

12 **MS. GLASSER:** Thank you.

13 **MR. COX:** Your Honor, you know, given the limitation
14 on time, I don't want to argue any further. I'll move on.

15 **THE COURT:** You can argue as much as you want.

16 **MR. COX:** We can impeach him whether it's hearsay or
17 not. And I wasn't seeking to introduce the document. I was
18 trying to lay a foundation. I was going into his analysis as
19 to whether it was a good time for an IPO, and that they were
20 going to make a ton of money in the first couple of weeks.

21 **THE COURT:** Well, impeach him by saying:

22 "Isn't it true other experts out there in the market
23 were saying it's a crappy time?"

24 **MR. COX:** No, not other experts. It's Ariosa's
25 investment bankers themselves were saying it.

1 **THE COURT:** We're saying that someplace else, but not
2 in the materials you looked at.

3 **MR. COX:** No.

4 **MS. GLASSER:** And Your Honor, we'd request the last Q
5 and A on that be stricken, where counsel made the
6 representation about the hearsay document.

7 **THE COURT:** Well, the witness brought up JPMorgan,
8 that's why I thought there was some JPMorgan material to work
9 with.

10 **MR. COX:** They were Ariosa's investment bankers.

11 But, Your Honor, I'll move on.

12 **THE COURT:** Okay.

13 **MR. COX:** I'm not --

14 **MS. GLASSER:** Is that acceptable, to strike the Q and
15 A where counsel made the representation about --

16 **THE COURT:** No.

17 **MS. GLASSER:** Okay. Really quick, Your Honor, I had
18 one additional topic --

19 **THE COURT REPORTER:** Could you kindly slow down?

20 **MS. GLASSER:** Actually, this doesn't even need to be
21 on the record, I don't think. It's just logistics on the jury
22 instructions.

23 **THE COURT:** Oh, okay.

24 **MR. COX:** Your Honor, time is very limited. I don't
25 want to start losing our time by arguing jury instructions.

1 **MS. GLASSER:** No. No.

2 (Discussion off the record.)

3 (Recess taken from 2:10 p.m. until 2:25 p.m.)

4 (Proceedings were heard in the presence of the jury:)

5 **THE COURT:** So --

6 **MR. COX:** Your Honor, we are going to pass the
7 witness.

8 **THE COURT:** All right. Anything else?

9 **MS. GLASSER:** No further questions.

10 **THE COURT:** Thank you very much, sir. You may step
11 down.

12 **THE WITNESS:** Thank you.

13 **MR. REINES:** Plaintiffs call --

14 **THE COURT:** Have you rested?

15 **MR. REINES:** That's my understanding.

16 **MR. GINDLER:** Yes. Ariosa rests.

17 **THE COURT:** Okay. Yes. Mr. Reines.

18 **MR. REINES:** Thank you. Plaintiffs call as their
19 rebuttal witness Dr. Cooper.

20 (Whereupon a document was tendered to the Court.)

21 **THE CLERK:** Raise your right hand.

22 **GREGORY MICHAEL COOPER,**

23 called in rebuttal as a witness for the Plaintiff, having been
24 duly sworn, testified as follows:

25 **THE WITNESS:** I do.

1 **THE CLERK:** Thank you. Go ahead and just state your
2 name again.

3 **THE WITNESS:** Gregory Michael Cooper.

4 **THE COURT:** Counsel, you may proceed.

5 **DIRECT EXAMINATION**

6 **BY MR. WALTER**

7 **Q.** All right. Dr. Cooper, you formed a series of rebuttal
8 opinions in this case. Can you please summarize for the jury
9 what these rebuttal opinions are?

10 **A.** Sure. So in my opinion, Drs. Oliphant and Stuelpnagel are
11 inventors on the '794 patent; that Straus neither anticipates
12 nor renders obvious the '794 patent; that the '430 patent
13 satisfies the written description and enablement requirements
14 for validity; and that Harmony™ infringes the '794 and '430
15 patent.

16 **Q.** All right. We're going to start with the inventorship
17 issue. Now, you've heard Dr. Oliphant and Dr. Stuelpnagel
18 contend that they're not inventors on the '794 patent.
19 Correct?

20 **A.** That's correct.

21 **Q.** You haven't heard from other expert, but you've heard that
22 from Dr. Oliphant and Stuelpnagel?

23 **A.** That's correct.

24 **Q.** What is your response to that?

25 **A.** I disagree.

1 Q. You've got a number of reasons why you think they actually
2 are inventors on the '794 patent. I'd like to walk through
3 some of those reasons. One of those reasons pertains to the
4 Golden Gate product?

5 A. Yeah.

6 Q. Can you explain what it is about the Golden Gate product
7 that supports your opinion that they're inventors?

8 A. Sure. So the other day I talked about and walked through
9 the Golden Gate product offered by Illumina, and how, in my
10 opinion, it very clearly embodies or practices the '794 patent.
11 And Dr. Oliphant, in this deposition testimony, clearly
12 testifies to the fact that he believes he, along with
13 Dr. Stuelpnagel, are inventors on Golden Gate. And so it
14 simply stands to reason they invented Golden Gate. Golden Gate
15 embodies the '794. That makes them inventors on the '794.

16 Q. All right. Now, that was a high-level reason for why you
17 believe they're inventors. You also looked specifically at
18 what they said they invented. And I'd like you to explain to
19 the jury how that supports your opinion.

20 A. Sure. So we heard a lot. And they were very specific
21 that their contribution related to this concept of extension
22 and ligation. So this is deposition -- or testimony from a
23 deposition from Dr. Oliphant.

24 And you heard something similar here at trial from both
25 him and Dr. Stuelpnagel about the importance of their singular

1 idea of extension and ligation.

2 Q. Now, is this idea in the claims?

3 A. Yes, absolutely.

4 Q. Okay. Where is it in the claims?

5 A. So you can see here in Claims 19 and 20, both of these
6 explicitly talk about the methods that involve extending and
7 ligating probes; so here, multiple claims are capturing what
8 they describe as their singular invention.

9 Q. Now, is this concept present in other claims, as well?

10 A. Yes. At the very least, you can see that these are
11 dependent claims on 9, 11, or 13, which, in turn, inherit from
12 Claim 1; so clearly there are multiple claims that they're
13 inventors on.

14 Q. So is this extension and ligation a preferred embodiment
15 of Claim 1?

16 A. Yes.

17 Q. All right. Now, one of the things they said they invented
18 was this concept of allele-specific extension and ligation. Do
19 you recall that?

20 A. I do recall it.

21 Q. Now, is that in the patent?

22 A. Yes, it is.

23 Q. Okay. Where is it in the patent?

24 A. At the very least, here in Figure 13. So this is a figure
25 in the '794 patent that, again, refers to -- talks about

1 extension and ligation. And they're showing you here a
2 schematic where they're talking about looking at a specific
3 site -- an allele-specific site -- in an allele-specific way.

4 Q. Now, how does the description within the text of the
5 specification describe this?

6 A. Well, it describes it as allele-specific extension and
7 ligation. And it talks about genotyping. It talks about --
8 and it clearly associates with Claims 19 and 20.

9 Q. Are there any other claims it corresponds to?

10 A. I believe this might be associated with Claim 2.

11 Q. Any other claims?

12 A. And certainly Claim 1 is also at play here.

13 Q. Is that a preferred embodiment of Claims 19 --

14 Is allele-specific extension and ligation a preferred
15 embodiment of Claim 1?

16 A. Yes.

17 Q. Now, you talked about allele specificity. How often is
18 that mentioned in the patent?

19 A. I believe many, many times.

20 Q. Do you recall the number, off the top of your head?

21 A. Maybe 60 or 70, if I recall. I can't remember exactly.

22 Q. What does that tell you about whether Arnold Oliphant and
23 John Stuelpnagel are inventors?

24 A. Well, it's very clearly the subject matter that they were
25 concerned with; that they contributed to. And it's covered in

1 the '794 patent.

2 Q. And again, which claims do you believe Figure 13
3 corresponds to, at a minimum?

4 A. Nineteen and twenty, certainly.

5 Q. And why do you believe that?

6 A. Well, certainly it provides a schematic of the language of
7 the claimed inventions; but we've also heard testimony here at
8 trial, including from Dr. Cantor, for example, about his belief
9 that it associates with Claim 19 and 20.

10 Q. Now, one of the other things we've heard from
11 Drs. Oliphant and Stuelpnagel is that they are not inventors on
12 the patent, because their invention is limited to something
13 that requires perfect complementarity. Do you recall that?

14 A. I do.

15 Q. All right. Now, does this argument of perfect
16 complementarity change your opinion as to whether they're
17 inventors or not?

18 A. No.

19 Q. Okay. Why not?

20 A. Well, because -- there's a number of reasons. The patent
21 describes, for example, definitions of complementarity.

22 So here is, for example, a specific definition of
23 "substantially complementary." And it talks about the fact
24 that hybridization has to occur if there --

25 In other words, substantially complementary occurs if

1 hybridization occurs.

2 And they talked a lot about the fact that if the allele --
3 a specific allele hybridizes, then the assay becomes
4 allele-specific, and works. And so, clearly, the patent
5 defines this.

6 And furthermore it's plain that if something is perfectly
7 complementary, it's also substantially complementary. So
8 "perfect" is in some sense a subset or a part of "substantially
9 complementary."

10 **Q.** Now, one of the claims that's been discussed often here is
11 Claim 2 of the patent.

12 **A.** Mm-hm.

13 **Q.** Can you describe --

14 Now, let me just ask a foundational question. Which of
15 the claims refer to substantial complementarity, if any?

16 **A.** At least Claim 2.

17 **Q.** Okay. Are there others that refer to it?

18 **A.** I believe there might be some, yes.

19 **Q.** Okay. Do all of the claims refer to substantial
20 complementarity?

21 **A.** No, I don't believe so.

22 **Q.** All right. Now, let's talk about Claim 2. Can you
23 describe for the jury what Claim 2 pertains to?

24 **A.** So Claim 2 introduces this idea of a detection and an
25 interrogation position, whereby you need complementarity at

1 that position to then proceed with the experiment.

2 **MR. WALTER:** And, Mr. Bonini, why don't you bring up
3 513, page 53, and highlight Claim 2.

4 (Document displayed.)

5 **BY MR. WALTER**

6 **Q.** Okay. So you referred earlier to -- this refers to a
7 detection position?

8 **A.** Correct.

9 **Q.** And what is the most natural interpretation of this?

10 **A.** Yeah. So the simplest interpretation -- and I believe we
11 heard Dr. Quackenbush say something to the same effect -- is
12 talking about a single base.

13 And this is the method or the claim that really focuses on
14 SNP genotyping -- we've heard a lot about that -- where you're
15 very interested in one, a single nucleotide, or a
16 single-nucleotide polymorphism, or "SNP."

17 And at such a position, the bases are either
18 complementary, or they're not. Right?

19 So A is complementary to T. C is complementary to G.

20 And in that circumstance, you're going after a SNP. The
21 probe is either complementary to that position, or it's not.
22 So there's no difference. There's literally no difference in
23 this context between "perfectly complementary" and
24 "substantially complementary."

25 **Q.** And what implication does that have for your opinion as to

1 whether Dr. Stuelpnagel and Oliphant are inventors on the '794
2 patent?

3 **A.** Well, this would certainly lead one to an allele-specific
4 product.

5 **Q.** And what implication does that have for your opinion as to
6 whether they're inventors?

7 **A.** And, again, that's clearly what they associated themselves
8 with.

9 **Q.** All right. Dr. Cooper, I'd like to move on now to the
10 Straus reference. You heard earlier today Dr. Cantor contended
11 that the Straus reference anticipates the '794 patent. Do you
12 agree with Dr. Cantor?

13 **A.** No.

14 **Q.** All right. Now, you understand one of the things he
15 relied upon most heavily was Figure 5?

16 **A.** That's right.

17 **MR. WALTER:** All right. Mr. Bonini, could you bring
18 up Figure 5, which is 1044, page 6?

19 (Document displayed.)

20 **BY MR. WALTER**

21 **Q.** All right. So this is Figure 5 that Dr. Cantor relied
22 upon today?

23 **A.** Yes.

24 **Q.** What's not disclosed in Figure 5?

25 **A.** Well, at a minimum, the level of multiplicity. That '794

1 patent talks about more than 100. There's simply no indication
2 in this figure as to the scale of experimentation. And, if
3 anything, it suggests -- you can see at the array at the bottom
4 there's 48 spots on that array, which is clearly suggesting a
5 level of multiplexing far below the '794 minimum.

6 **Q.** Now there's also some figures here. What does that tell
7 you about the level of multiplicity in this patent, if
8 anything?

9 **A.** Again, indicating handfuls of -- of targets here.

10 **Q.** Now, what about the number of priming sites?

11 **A.** It says nothing about how many primers one might use in
12 this figure.

13 **Q.** All right. Now, you recall Dr. Cantor relied on paragraph
14 39 of Straus to contend that there were the required number of
15 probes that were used?

16 **A.** I do.

17 **Q.** Do you recall that testimony?

18 **MR. WALTER:** All right. Mr. Bonini, could you please
19 bring up paragraph 39, which is on page 16?

20 (Document displayed.)

21 **BY MR. WALTER**

22 **Q.** Now, does paragraph 39 -- does this ever refer to
23 Figure 5?

24 **A.** Not as far as I could tell. There was no connection to
25 Figure 5.

1 Q. Okay. Did Dr. Cantor ever provide any reason why you
2 combined this disclosure with Figure 5?

3 A. No, not that I heard.

4 Q. Okay. Now, what's your -- just to clarify the importance
5 of that, what's your understanding of what's required for
6 anticipation?

7 A. My understanding is that all of the elements of the claim
8 have to be in one disclosure or figure, and they have to be
9 arranged in the same configuration.

10 Q. All right. Now looking at paragraph 39, does it support
11 or contradict your opinion that Straus anticipates or does not
12 anticipate the '794 patent?

13 A. I believe it's leaning towards not anticipating,
14 absolutely.

15 Q. Why is that?

16 A. So it certainly talks about more than 50 or more than 250
17 different amplifiable probes; but it puts it in the context of
18 talking about doing this in the -- that the probes include more
19 than five families of amplified probes.

20 And my understanding after reading the patent is it talks
21 a lot about families or sets of things. And in particular it's
22 referring to sets of different infectious organisms, so maybe
23 it's certain taxa of viruses or bacteria. And there are lots
24 of reasons one might separate those into groups. And I think
25 the families of amplifiable probes is key here. You amplify

1 each one of them with a separate strategy or sequence.

2 **Q.** All right. Now, can a distinction be made between having
3 an identical universal priming site, and having multiple
4 universal priming sites?

5 **A.** Yes.

6 **Q.** Okay. And how does that distinction pertain to the
7 testimony you just made regarding the families and the taxa?

8 **A.** Well, this, to me, suggests that they're using collections
9 of amplifying sites; so collections of multiple sites, as
10 opposed to an identical universal priming site across all of
11 the targets, as specified in the '794.

12 **MR. WALTER:** All right. Now let me show you
13 paragraph 22 of the Straus reference, which is on page 1044-15,
14 upper right-hand corner.

15 (Document displayed.)

16 **BY MR. WALTER**

17 **Q.** So this is a paragraph -- this is the first paragraph of
18 the Summary of Invention of Straus.

19 **A.** Mm-hm.

20 **Q.** Can you describe for the jury what this pertains to, and
21 how this supports your opinion that the '794 patent is not
22 anticipated?

23 **A.** Yeah. So this really kind of talks about how they're
24 looking for a strategy that's diagnostic of numerous different
25 types of organisms. And this gets back to what I said earlier

1 about assembling groups of organisms that are related to one
2 another; so maybe a set of E. Coli strains, or a set of viral
3 strains. And those might have very different genetic or
4 sequence properties. So a simple example is their GC-content.

5 So we talked about DNA has four letters: A, T, G, and C.
6 And some organisms, especially viruses and bacteria, can have
7 extreme GC, or extreme levels of AT. And what that means is
8 that they amplify with very different characteristics. And
9 that's why you might, in fact, use this kind of method where
10 you're amplifying differently for each one of those groups.

11 **Q.** All right. Now let's continue to follow up on that. One
12 of the things Dr. Cantor testified about was that the
13 requirement for 100 different target sequences was met by
14 something called "ID sequences."

15 (Reporter requests clarification.)

16 **MR. WALTER:** ID sequences. Yeah. ID sequences.

17 And that's in paragraph 138, which is on 1044-25.

18 (Document displayed.)

19 **BY MR. WALTER**

20 **Q.** And actually, I'm going to move to something pretty quick;
21 something else, actually.

22 Just looking at those ID sequences -- just this reliance
23 on ID sequences -- does that support your opinion that the '794
24 is not anticipated?

25 **A.** Yes. In a number of spots in the Straus patent it

1 actually talks about synthesizing primers, or each ID probe or
2 group of ID probes, again, clearly suggesting you use multiple
3 sets of amplification sequences.

4 **MR. WALTER:** All right. I'm going to point you to
5 one example of that. It's 1044-40.

6 And if you could, bring up paragraphs 359 and -60.
7 (Document displayed.)

8 **BY MR. WALTER**

9 **Q.** All right. Could you elaborate for the jury what you're
10 referring to here?

11 **A.** So here at 360 it says for each ID sequence, a pair of ID
12 probes and a pair of primers are synthesized; again, talking
13 about -- clearly teaching towards multiple different
14 amplification sequences.

15 **Q.** All right. So again, does the Straus reference teach an
16 identical universal priming site, as required by the claims of
17 the '794 patent?

18 **A.** No.

19 **Q.** Okay. Does Figure 5 teach the level of multiplicity, as
20 required by the '794 patent?

21 **A.** No.

22 **Q.** How many different spots are on that array that are shown
23 at Figure 5?

24 **A.** I believe there are 48; far less than 100.

25 **Q.** That's not greater. Far less than 100. All right.

1 I'd like to move on, now, to infringement issues on the
2 '794 patent. Now, you were here for Dr. Quackenbush's
3 testimony today?

4 A. I was.

5 Q. He never gave an opinion that in Harmony™, there was not
6 more than 100 single-stranded target sequences attached to a
7 solid support. Is that right?

8 A. I did not hear one.

9 Q. Now, one of the things that did come up during
10 Dr. Quackenbush's testimony was some testimony by Dr. Zahn. Do
11 you recall that?

12 A. I do.

13 Q. And for the jury, again, who is Dr. Zahn?

14 A. Dr. Zahn was a Lead Scientist at Ariosa in developing
15 Harmony™.

16 Q. And do you recall what testimony was discussed during
17 Dr. Quackenbush's?

18 A. I believe Dr. Zahn mentioned that he believed that the
19 vast majority of target sequences would be bound after the
20 two-hour annealing step.

21 Q. All right. And why does that --

22 Does that support your opinion that the requirement that
23 there be more than a hundred single-stranded target sequences
24 attached to a solid support is satisfied?

25 A. Absolutely, because it's, in fact, very similar to my

1 estimate of 99 percent, which I put in as an admittedly
2 imprecise estimate, but one that I felt was germane to the
3 question of whether or not there were more than 100, because
4 99 percent leads you to the conclusion that there are a hundred
5 thousand. And clearly, Dr. Zahn believes the vast majority,
6 which is very different than saying all or nearly all of them.

7 **Q.** So what does that tell you about whether that annealing
8 reaction proceeds to completion?

9 **A.** That it is unlikely to proceed to completion; that they
10 focused on specificity of hybridization, not sensitivity.

11 **Q.** Is there any other evidence that supports your opinion to
12 that effect?

13 **A.** We talked about a lot of that evidence, yes; about the
14 temperatures; about Dr. Zahn stating clearly that they
15 maximized specificity.

16 **Q.** All right. Now, one of the other things that
17 Dr. Quackenbush suggested during his testimony today was that
18 70 degrees Celsius would still be hybridization between the
19 oligos and the DNA. Do you recall that testimony?

20 **A.** I do.

21 **Q.** Do you agree with him?

22 **A.** Absolutely not.

23 **Q.** All right. Now, to your knowledge, did Quackenbush try to
24 provide any information regarding the melting temperatures of
25 the oligos that are used in Harmony™?

1 A. I don't believe so.

2 The only testimony I heard on this point was the
3 hybridization of the universal PCR primers, which are very
4 different oligos; and different in terms of their binding
5 properties to the actual DANSR assay oligos.

6 Q. Now you did, in your Expert Report, provide information
7 regarding the melting temperatures of the oligos?

8 A. That's right.

9 Q. What did you find?

10 A. I was provided DANSR assay oligos, and I estimated their
11 melting temperatures. So just --

12 A melting temperature is a standard, widely used concept
13 in molecular biology. And it describes the temperature at
14 which half of the double-stranded -- so the duplexes -- would
15 disassociate into single strands.

16 So when you're above that temperature, it's too warm, and
17 most of them are, in fact, single-stranded.

18 And only when you get below that temperature do you sort
19 of prefer the duplex formation.

20 So I estimated the melting temperature of the DANSR assay
21 oligos.

22 Q. How did you do that?

23 A. I used several different tools that approach it. There
24 are a variety of similar ways; but I did it, actually, with
25 multiple tools, but focused on one called "nearest-neighbor

1 two-state model."

2 Q. All right. And how many oligos did you look at?

3 A. A couple thousand.

4 Q. And what did you find?

5 A. That the melting temperatures ranged from 55 to 65 degrees
6 Celsius, and they were clustered right around 60.

7 Q. And was it enough for you to only measure 2,000?

8 A. Yes, because that is a large fraction of them; and also
9 they've stated quite clearly that they designed their assay to
10 have uniform melting temperatures, which is to say as similar
11 as they can be across all of the oligos, which is consistent
12 with their literature and also consistent with somewhat
13 standard practice in this field.

14 MR. WALTER: Can you please bring up 462-2? And it's
15 paragraph under "Digital Analysis of Selective Regions Assay."

16 THE COURT: What exhibit is this?

17 MR. WALTER: This is Exhibit 462.

18 THE COURT: Right, which is what?

19 MR. WALTER: It's a paper. Yeah.

20 (Document displayed.)

21 BY MR. WALTER

22 Q. Can you identify it for the jury?

23 A. Yes. This is a scientific manuscript published by Ariosa
24 scientists.

25 Q. Okay. All right. And you talked about the uniform

1 melting temperatures?

2 **THE CLERK:** Is this sealed?

3 **MR. WALTER:** No.

4 **THE WITNESS:** That's correct. So clearly they're
5 saying here they selected loci based upon having uniform
6 Locus-Specific Oligo melting temperatures.

7 **BY MR. WALTER**

8 **Q.** All right. Now, when Dr. Quackenbush said you made
9 mistakes in your determination as to the single-stranded target
10 sequence claim element, what's your response?

11 **A.** Well, I disagree. And I estimated the melting
12 temperatures. And 70 is well above the melting temperatures of
13 these oligos. So when they heat them to 70, they will
14 disassociate, by and large. And those target sequences will be
15 single-stranded, and affixed to the beads.

16 **Q.** Now, Dr. Cooper, I want to move on now to the issue of
17 Readout Cassettes and amplicons.

18 **A.** Mm-hm.

19 **Q.** You heard some testimony from Dr. Quackenbush earlier that
20 Readout Cassettes weren't amplicons. Do you recall that?

21 **A.** I heard that. Yeah.

22 **MR. WALTER:** Could you bring up -- excuse me -- 422?
23 (Document displayed.)

24 **BY MR. WALTER**

25 **Q.** And what is this document, Dr. Cooper?

1 A. It appears to be a Standard Operating Procedure document.

2 MR. GINDLER: Can we get one of those documents?

3 MR. WALTER: Go ahead.

4 THE CLERK: These numbers show -- I see them sealed.

5 I don't know if portions are sealed. Okay.

6 MR. GINDLER: It's this one.

7 THE CLERK: I had the other one down, too, so I don't
8 know.

9 (Discussion off the record.)

10 BY MR. WALTER

11 Q. All right. Dr. Cooper, what is this document?

12 A. An SOP document for Harmony™.

13 MR. WALTER: All right. Mr. Bonini, could you
14 magnify the "Purpose" paragraph? And can you highlight,
15 "Purified PCR Amplified Product"?

16 (Document displayed.)

17 BY MR. WALTER

18 Q. All right. What is this paragraph describing?

19 A. It's just making plain the purpose of this is to put
20 amplicons or amplified PCR product onto the -- hybridized to
21 the array.

22 Q. And this is describing what happens in Ariosa's product?

23 A. It is.

24 Q. Now, does the term "PCR amplified product" -- is that an
25 amplicon?

1 A. It's a very plain definition of amplicon. Yes.

2 Q. Can you explain whether that meets the Court's
3 construction of "amplicon," or not?

4 A. It absolutely does.

5 Q. Okay. Can you explain why?

6 A. Because the Court's construction talks about an amplicon
7 being the product of amplification.

8 Q. Now, you heard about -- Dr. Oliphant testified that for
9 something to be an amplicon, it needs to be something that can
10 be amplified. Do you recall that?

11 MR. HEINRICH: Objection. He's mischaracterizing
12 Dr. Oliphant's testimony, and he shouldn't be characterizing
13 it.

14 THE COURT: Well --

15 MR. WALTER: I suppose they can redirect him and
16 cross-examine if they think I've mischaracterized it. I think
17 I'm characterizing it pretty fairly.

18 THE COURT: And the jury's going to have to recall
19 what it heard. I'm just concerned this is all very specified
20 stuff. So are you reading from a transcript?

21 MR. WALTER: I'm not reading from the transcript, but
22 I would like to respond to their arguments. And I believe one
23 of their arguments is that an amplicon needs to be something
24 that was amplified.

25 THE COURT: All right. You can ask him if he heard

1 that.

2 **BY MR. WALTER**

3 **Q.** Did you hear Dr. Oliphant say that he believed an amplicon
4 should be something that can be --

5 (Reporter requests clarification.)

6 **MR. WALTER:** Well, let me try it again. Let me just
7 ask it generically.

8 **Q.** If someone were to tell you that an amplicon is something
9 that must be capable of being amplified, would you agree with
10 that?

11 **A.** No.

12 **Q.** What is an amplicon?

13 **A.** I believe an amplicon is the product of amplification. It
14 might also have the ability to lead to more amplification, but
15 that's not a requirement. It's the product of amplification.

16 **Q.** Is a Readout Cassette an amplicon?

17 **A.** Absolutely.

18 **Q.** Why?

19 **A.** Because it's an amplicon. It's produced from PCR
20 amplification.

21 **Q.** Okay. Now, the other thing that we heard about is
22 arguments regarding infringement of the '430 patent.

23 **A.** Mm-hm.

24 **Q.** Do you recall that? Do you recall Dr. Quackenbush's
25 arguments regarding the '430 patent?

1 A. I do.

2 Q. And there were two basic arguments. The first one was
3 that they don't use sequence reads. Do you recall that?

4 A. I do.

5 Q. And do you recall testimony yesterday from Dr. Wang, where
6 he talked about quantile normalization?

7 A. I do.

8 Q. Does any of that testimony change your opinion as to
9 whether there was infringement?

10 A. No. They're clearly still using sequence reads.

11 Q. Is a normalized enumerated sequence read still a sequence
12 read?

13 A. Yes, absolutely. And again, they're still using the reads
14 as part of this process in a very plain and straightforward and
15 commonsense way. The reads are used.

16 Q. What is a normalized sequence read, as opposed to a
17 non-normalized sequence read?

18 A. It's a sequence read that's been subject to some cleaning
19 up and processing that is very standard in this kind of field.

20 Q. Now, another thing that they argued was that FORTE doesn't
21 use a reference chromosome. Do you recall that?

22 A. I do.

23 Q. Okay. Do you agree with that?

24 A. No.

25 Q. All right. Now, why do you disagree with that?

1 A. Because they compute proportions or comparisons of the
2 test chromosomes -- so 21, for example -- to multiple other
3 chromosomes; 18 and 13, for example.

4 Q. And what evidence supports that that you have heard and
5 seen?

6 A. So we've talked about deposition testimony from Dr. Wang.
7 And yesterday he actually said that we use reads from
8 Chromosome 18 when we're testing Chromosome 21.

9 And when Dr. Quackenbush drew this figure, he put this
10 proportion metric that includes 21 in the numerator, 13 and 18
11 in the denominator, using reference chromosomes.

12 Again, to me, this is a very commonsense understanding of
13 the assay.

14 Q. Can you explain what that "P" is in this slide?

15 A. Yeah. It's proportions.

16 Q. And is that a comparison?

17 A. Yes.

18 Q. What's being compared here?

19 A. Chromosome 21 to -- a test chromosome, to a reference
20 chromosome.

21 Q. What are the reference chromosomes here?

22 A. Thirteen and eighteen.

23 Q. All right. Now, you also looked at source code in this
24 case. Correct?

25 A. That's right.

1 Q. Did Dr. Wang or Dr. Quackenbush show any source code?

2 A. No, I do not believe so.

3 MR. WALTER: Okay. I'd like to take a quack look at
4 some of that source code, again. Can I have the Elmo? Yeah.
5 I have the power on.

6 (Document displayed.)

7 BY MR. WALTER

8 Q. All right. Now this was a source-code file we looked at
9 earlier in the case.

10 A. Uh-huh.

11 Q. Okay. Now, what is this source code for?

12 A. It's called "compare locus classes," where they do a
13 comparison of the difference sequence reads from different
14 chromosomes.

15 Q. Okay. Now, there's a loop down here that begins -- that
16 says, *Analyze a dataset to compare locus classes*. Do you see
17 that?

18 A. Mm-hm. Yes, I do.

19 Q. Okay. What are the locus classes?

20 A. Those are the different loci from different chromosomes of
21 interest.

22 Q. What is the name of this source-code file?

23 A. "Compare locus classes."

24 Q. Okay. So what's happening in this source-code file?

25 A. This is where they're --

1 For each chromosome of interest -- so, say, 21 -- they're
2 comparing it to collections of reads from data from multiple
3 other chromosomes in the denominator.

4 **MR. WALTER:** All right. I'm going to show you the
5 next page of the source-code file.

6 (Document displayed.)

7 **BY MR. WALTER**

8 **Q.** Do you see here where it says, "compute the denominator
9 component means"?

10 **A.** I do.

11 **Q.** Okay. And then below it says "compute proportions"?

12 **A.** I do.

13 **Q.** Okay. And what's being computed there?

14 **A.** These are the chromosomal proportions, as drawn out.

15 **Q.** I'd like to finish off with the enablement issues.

16 **A.** Okay.

17 **Q.** You heard Dr. Cantor present an opinion that the '430
18 patent wasn't enabled, or couldn't be used by someone of skill
19 in the art for its intended purpose?

20 **A.** I did.

21 **Q.** Do you agree with that?

22 **A.** I do not.

23 **Q.** Why do you disagree?

24 **A.** Because the patent provides an extensive amount of -- of
25 language, of figures, of citations that all provide the

1 information necessary to perform the claims.

2 **MR. WALTER:** All right. So what I'd like to do is
3 look at some of the figures in the patent in just a little bit
4 more detail.

5 Mr. Bonini, could you please put up 514-5?

6 (Document displayed.)

7 **BY MR. WALTER**

8 **Q.** Now, one of the arguments you heard from Dr. Quackenbush
9 was there would be an issue with being able to enrich the
10 number of sequences. Do you recall that?

11 **A.** I do.

12 **Q.** Okay. What is Figure 1 showing?

13 **A.** Well, I believe this is referring to the selection
14 strategy for designing the -- the loci. This is, I believe,
15 talking about the hotspots.

16 But what it's doing is it's giving you a step-by-step sort
17 of instruction about the order of the steps that one needs to
18 collect some information, identify the spots along the target,
19 and then to proceed through the process. So it's giving some
20 detailed information.

21 **MR. WALTER:** All right. Now let's look at Figure 11
22 now, which is 514-16.

23 (Document displayed.)

24 **BY MR. WALTER**

25 **Q.** What is this figure showing?

1 **A.** So I believe this is talking about a different strategy
2 for selecting targets, called "chromosome walking." And it
3 says we're interested in this Down Syndrome critical region,
4 for obvious reasons. You have this FASTA data. It's just a
5 file -- a particular file format that's common.

6 It says "Primer-BLAST." That's, you know, a form of a
7 program that lots of genomicists use.

8 It tells you how many to design; that they should be
9 unique 21. They should be a certain size range.

10 So it's giving you lots of information about designing the
11 assay.

12 **Q.** Would someone of skill in the art, based on the disclosure
13 in the patent, be able to implement the chromosome or hotspot
14 invention to carry out the claimed invention?

15 **A.** Yes.

16 **MR. WALTER:** Now, there was also this issue of
17 possession. And Dr. Cantor was a little bit unsure whether the
18 inventors were in possession.

19 But what I'd like to have you do is look at Figure 23,
20 which is 514-29.

21 (Document displayed.)

22 **BY MR. WALTER**

23 **Q.** What does this tell you about whether the inventors were
24 in possession of the invention?

25 **A.** So what they're showing you here is on this figure, along

1 the x-axis -- the horizontal axis -- is a portion of the human
2 genome of Chromosome 21.

3 And then the y-axis here, these black vertical bars are
4 showing you read counts; so how many reads they collected.

5 So this is clearly demonstrating that they performed an
6 enrichment. They put them on the sequencers. They collected
7 and analyzed a bunch of data.

8 Q. All right. So the other argument they raised was that the
9 information regarding the bioinformatics was not adequate. Do
10 you recall that?

11 A. I do.

12 MR. WALTER: All right. Mr. Bonini, could you bring
13 up 514, 39, column 13, line 49? Line 49.

14 (Document displayed.)

15 BY MR. WALTER

16 Q. All right. Now, this is a passage that was referred to
17 that describes techniques for determining fetal aneuploidy?

18 A. It is.

19 Q. What kind of techniques are described in these references?

20 A. That's actually a variety of statistical methods, ranging
21 in sophistication, including things like Z scores, and other
22 methods for doing analysis of this data.

23 Q. Okay. Please take a look at Tab 507A in your binder.

24 A. Okay.

25 Q. What is 507A?

1 A. This is a patent publication. A patent application
2 publication.

3 Q. Do you know if that's one of the references that's
4 incorporated by reference into the '430 patent?

5 A. Yes, I believe it is.

6 MR. WALTER: I'd like to have Exhibit 507A admitted
7 into evidence.

8 MR. HEINRICH: No objection.

9 THE COURT: Thank you --
10 (Trial Exhibit 507A received in evidence.)

11 MR. WALTER: Okay. Please bring up 507A, paragraph
12 64, on page 15, Mr. Bonini.

13 (Document displayed.)

14 BY MR. WALTER

15 Q. What's being described in this paragraph?

16 A. So this is talking about how to compute cutoff parameters,
17 and describes other types of methods. So as one example, it
18 talks about a Bayesian-type likelihood method as an example.

19 Q. Why do you find that relevant?

20 A. Because when you heard Dr. Wang speak yesterday about
21 FORTE, he talked about this notion of prior probability. So
22 maternal age, for example, is a prior probability that FORTE
23 uses to change the output.

24 That's what is meant by a Bayesian analysis. So a
25 Bayesian characterization is when you use prior information to

1 help dictate the outcome of the posterior information.

2 It also talks about a likelihood method. And again, we
3 heard from Dr. Wang and Dr. Quackenbush today about this
4 disomic versus trisomic model. That's a likelihood model. So
5 that's very much the general class of methods that FORTE is
6 using.

7 **Q.** Now, you know, there was also this issue of normalization.
8 Is normalization incorporated by reference into some of the
9 disclosures that are in this patent -- in the '430 patent?

10 **A.** It does.

11 And I should also say that normalization techniques were
12 well known to people of ordinary skill in the art at this time
13 frame. I've had lots of experience personally, for example.

14 **Q.** All right. Now, you heard testimony from both Dr. Cantor
15 and Dr. Wang that they thought the types of techniques
16 disclosed in the '430 patent, like a Z score, wouldn't work.
17 Do you recall that testimony?

18 **A.** I do.

19 **Q.** Do you agree with it?

20 **A.** I don't.

21 **Q.** Why not?

22 **A.** Because Ariosa scientists published an analysis based upon
23 Z scores that was quite effective.

24 **MR. WALTER:** Okay. Can you bring up Document 462?

25 (Document displayed.)

1 BY MR. WALTER

2 Q. Is this the document you're referring to?

3 A. Yes. It looks like it.

4 MR. WALTER: Okay. Can you magnify the authors and
5 the title? Okay.

6 (Document displayed.)

7 BY MR. WALTER

8 Q. Who's the second author on this paper?

9 A. Dr. Wang, that we heard from yesterday.

10 Q. All right. And what, if anything, does this paper say
11 about whether they detect Trisomy 21 and 18?

12 A. It says that they were quite effective and accurate in
13 detecting those trisomies.

14 MR. WALTER: Could you bring up 462-6?

15 On the lower right hand there's a, "What Does This Study
16 Add?" Can you highlight that?

17 (Document displayed.)

18 BY MR. WALTER

19 Q. All right. And what does this say?

20 A. That this study demonstrates non-invasive detection of
21 Trisomy 21 and 18 using selective sequencing of cell-free DNA
22 from specific chromosomes.

23 Q. Now, does this paper use FORTE?

24 A. No.

25 Q. What does it use?

1 A. It primarily relies on Z scores.

2 Q. Now, one thing I want to come back to is this issue of
3 reference chromosomes. Did the Court have anything to say in
4 its Claim Construction Order about what reference chromosomes
5 could serve as references for test chromosomes?

6 A. Yes. I believe it's stated plainly that --

7 MR. WALTER: Can I have the Elmo?

8 THE WITNESS: -- the potential chromosomes of
9 interest -- especially 21, 13, and 18 -- could also be used as
10 reference chromosomes.

11 BY MR. WALTER

12 Q. Okay. So I'm going to put that up. Can you see this down
13 here?

14 (Document displayed.)

15 MR. HEINRICH: Oh, objection.

16 THE COURT: Yeah. Just the construction.

17 MR. WALTER: Okay. All right. I'll pass the
18 witness.

19 CROSS-EXAMINATION

20 BY MR. HEINRICH

21 Q. Good afternoon, ladies and gentlemen. Good afternoon,
22 Dr. Cooper. Kind of in the home stretch here today, so I'm the
23 one that gets to keep us from the weekend.

24 All right. Why don't we start with Version 2 of Harmony™.
25 And do you agree that it's very important to make sure that

1 we're distinguishing between Version 1 and Version 2 of
2 Harmony™, because there are different infringement issues for
3 each version? Correct?

4 A. That's fair to say.

5 Q. Okay. And you gave some testimony earlier on your
6 rebuttal direct that applied to Version 1, and you gave some
7 testimony to Version 2. Correct?

8 A. Yes.

9 Q. Okay. And when you cited that paper, Exhibit 462, that
10 paper was before Version 2 even was created. Right? So that
11 was, if anything, related to Version 1. Is that fair?

12 A. Yes.

13 Q. Okay. And you also gave some testimony about Version 2
14 with respect to the amplicon concept. Correct?

15 A. I did.

16 Q. Okay. So why don't we start with the amplicons. So let's
17 just reorient ourselves. We have modified probes. Correct?

18 A. At some point during the assay, yeah.

19 Q. Right. And the Ariosa modified probes have a universal
20 priming site; a sequence that's complementary to the target
21 sequence -- correct? -- and then a Readout Cassette. Correct?

22 A. Yes.

23 Q. In fact, the Ariosa probes have two different universal
24 priming sites: A left, and a right. Correct?

25 A. Yes.

1 Q. And that modified probe is then replicated, in whole. The
2 whole thing is replicated in Harmony™ V2. Correct?

3 A. Yes.

4 Q. And that's what the Court tells us is the amplification
5 product; the amplicon. Right?

6 A. No, I don't believe so.

7 Q. So the Court's construction is, *Wherein the different*
8 *modified probes are replicated, in whole or in part, to yield*
9 *amplification products of each of the different modified*
10 *probes*. That's the Court's construction. Correct?

11 A. Correct. And it says "amplification products of each of
12 the modified probes," so it doesn't say that they have to be
13 the same, exact molecule.

14 Q. Well, we know that it's the modified probes. If they're
15 replicated in whole, that's the amplification product. Right?

16 A. Well, no. That's one amplification product.

17 Q. Isn't it true --

18 A. There are multiple possible products.

19 Q. Isn't it true, sir, that Ariosa doesn't replicate only a
20 part of the modified probe; Ariosa replicates the entire
21 modified probe? Is that fair?

22 A. Sure.

23 Q. Okay. And the amplicon has everything that was amplified.
24 Correct?

25 A. At one stage in the process the amplicon has everything,

1 Yes.

2 Q. At some point you do produce an amplicon unit which has
3 everything that was amplified. Right?

4 A. Yes.

5 Q. Okay. So in Ariosa, everything that was amplified
6 includes the universal priming site, the sequence that's
7 complementary to the target -- actually, two universal priming
8 sites, and a Readout Cassette. Correct?

9 A. At one stage of the process, yes.

10 Q. Right. That's what's amplified? And that's also
11 amplifiable; isn't it?

12 A. Yes, it is.

13 Q. Okay. But that amplification product is never attached to
14 a second solid support in DANSR. Correct?

15 A. Not the whole thing, but an amplification product is.

16 Q. Not what's actually amplified. Isn't that fair?

17 A. No. The Readout Cassette is amplified.

18 Q. Not the whole thing is amplified. We amplified the entire
19 modified probe, but we don't attach the entire modified probe
20 that's amplified to the second solid support. Correct?

21 A. I feel like we're talking at odds. You're attaching an
22 amplicon.

23 Q. Sir, the Readout Cassette is the only thing that's
24 attached to the microarray. Correct?

25 A. Yes.

1 Q. The rest of the amplicon is destroyed. Correct?

2 A. Yes.

3 Q. Thank you. Now, were you here for Dr. Oliphant's
4 testimony that Ariosa -- where he testified that Ariosa
5 actually had actually tried but failed to attach an amplicon to
6 a microarray. Did you hear that?

7 A. I heard that he said they tried and failed to attach the
8 whole amplicon, yes.

9 Q. Do you have any reason to dispute his testimony?

10 A. No. I have no basis to agree or disagree with that.

11 Q. And you understand that the reason why it wasn't possible
12 to attach the entire -- to attach the amplicon to the array was
13 because it had poor kinetics, and it interfered with other
14 neighbors, it was hybridizing improperly, and not providing a
15 good signal? You understood that. Right?

16 A. I mean, I think you're paraphrasing him; but that's,
17 again, his understanding.

18 Q. And you have no reason to dispute that. Correct?

19 A. I have no basis, either way.

20 MR. HEINRICH: All right. So you provided some
21 testimony about melting temperatures. I think you cited
22 Exhibit 462. And if we could actually call up 462.
23 (Document displayed.)

24 BY MR. HEINRICH

25 Q. I want to just make sure that we're really clear here. So

1 this is not an actual SOP from Ariosa. Correct?

2 A. I don't know.

3 Q. You don't know?

4 A. No. I said "No."

5 Q. Okay. Okay. And this paper was published back in --
6 what? -- 2012? Is that your understanding?

7 A. Yes.

8 Q. Okay. So the passage here that you were pointing out --
9 that passage was not about Version 2 of Harmony™. Correct?
10 That was about Version 1?

11 A. That's right.

12 Q. And so when we're talking about the 70 degrees, we're in
13 agreement that in Harmony™ Version 2, there's a two-hour step
14 for hybridization. Correct?

15 A. Yes.

16 Q. And do you now agree that the probes and beads are added
17 together at room temperature?

18 A. Yeah, and then taken into the annealing step to heat it up
19 to 70. Yes.

20 Q. Okay. So they are added together at room temperature.

21 Then they're put in a thermocycler. The temperature is
22 70 degrees Celsius. And it gradually lowers the temperature to
23 20 degrees Celsius over that two-hour time period. Correct?

24 A. I thought it ended at 30, but yes.

25 Q. Okay. And you agree that as the temperature drops,

1 everyone -- everyone -- you, Dr. Oliphant, Dr. Quackenbush --
2 there's at least agreement that there's a lot of hybridization
3 going on. And that's, in fact, the goal of this whole step.
4 Correct?

5 **A.** Yeah. I would say the goal is to get the majority of the
6 targets bound to their correct assay oligos.

7 **Q.** And the beads are not added until after that hybridization
8 step completes. Correct?

9 **A.** Well, as I mentioned, I don't think it completes; but
10 after the two hours are over, yes.

11 **Q.** Okay. So let's talk a little bit about the '430 patent.
12 Now, the claims of the '430 patent require enumerated sequence
13 reads. Correct?

14 **A.** That's right.

15 **Q.** And you understand that in the Harmony™ Version 1 test,
16 there are enumerated sequence reads that are input into the
17 FORTE algorithm. Correct?

18 **A.** I couldn't tell you precisely where FORTE begins and ends;
19 but yes, there are enumerated sequence reads that are used as
20 parts of the process of Harmony™.

21 **Q.** And you were here for Dr. Wang's testimony. Right?

22 **A.** I was.

23 **Q.** And Dr. Wang gave an example of one of the mathematical
24 transformations that FORTE does. Correct?

25 **A.** Yes. He talked about quantile normalization.

1 Q. And in quantile normalization, each and every one of those
2 enumerated sequence reads from each sample is simply changed.
3 Isn't that fair?

4 A. Well, I would say that quantile normalization is using
5 those reads, and transforming them into different numbers that
6 have properties that are essentially cleaner. It's cleaner
7 data. Yes.

8 Q. Every single value that comes out of the sequencer for a
9 particular sample at a particular locus is fundamentally
10 transformed through quantile normalization. Correct?

11 A. I'm not sure about the word "fundamental," but the
12 sequence counts are used by -- via normalization, yes, they are
13 transformed.

14 Q. And, in fact, it's a type of rank normalization. Correct?

15 A. Yes.

16 Q. So there's a median calculated across all 96 samples for
17 all of the loci. Correct?

18 A. Yeah. Rank normalization is a very common technique in
19 genomics.

20 Q. And that median represents the median value across all 96
21 samples for each locus. Correct?

22 A. Yes.

23 Q. And then every single sequence read -- every enumerated
24 read that comes out of the sequencer for each sample is
25 replaced with a median value that is calculated not for a given

1 sample, but across all 96 samples. Correct?

2 A. I don't think that's the way I'd put it.

3 I would say that it's used in a process of normalization
4 that leads to a new set of numbers.

5 Q. Now, do you disagree with how Dr. Wang explained how
6 quantile normalization works in FORTE?

7 A. No. I have no reason. I mean, he gave a simple overview
8 of the basics of median rank normalization.

9 Q. And you disagree with how Dr. Wang explained how FORTE
10 does the Monte Carlo simulations?

11 A. No.

12 Q. And do you disagree with how FORTE uses -- I'm sorry. Do
13 you disagree with how Dr. Wang explained how FORTE uses those
14 Monte Carlo simulations to calculate a risk score?

15 A. No.

16 Q. Okay. Why don't we change gears a little bit, and talk
17 about inventorship. You were here in court when
18 Dr. Stuelpnagel testified and Dr. Oliphant testified. Correct?

19 A. Yes.

20 Q. And you heard how they explained to the jury that their
21 specific contribution to the '794 patent was something called
22 "allele-specific extension ligation." Correct?

23 A. Yes.

24 Q. And do you dispute Dr. Stuelpnagel and Oliphant's
25 testimony that that is what their contribution was?

1 A. No. I dispute whether or not it's part of the '794.

2 Q. Okay, but you can accept that that's what they invented.

3 You're not here to comment on their credibility as witnesses.

4 Correct?

5 A. No. In fact, I relied upon their testimony in their

6 deposition, and here at trial.

7 Q. Okay, but in fact, when you -- and you also claimed that

8 because of their invention of allele-specific extension

9 ligation, they are properly named as inventors on the '794

10 patent and, in fact, are properly named as inventors on Claim 1

11 of the '794 patent. Is that right?

12 A. Yes, I believe that's correct.

13 Q. But when you provided your infringement analysis to the

14 ladies and gentlemen of the jury, at no point at all did you

15 say that in Harmony™, either Version 1 or Version 2 -- that

16 Harmony™ or the DANSR assay uses allele-specific extension

17 ligation. Isn't that fair?

18 A. The Harmony™ does not use the extension part. Yes.

19 Q. In fact, Harmony™ does not use allele-specific extension

20 and ligation. Correct?

21 A. It uses allele-specific reactions, but not the extension

22 part. Yes.

23 Q. Right, because the extension part is really the core of

24 what Dr. Stuelpnagel and Oliphant invented. Right?

25 A. I think that's part of it, yes.

1 Q. Because that was the point. Right? There was another
2 patent family that taught allele-specific ligation. And they
3 designed around that patent by coming up with their invention
4 of allele-specific extension and ligation. Correct?

5 A. That sounds like a paraphrase of the testimony they gave.
6 Yes.

7 Q. Okay. So we're very clear that there's no allegation here
8 that either Version 1 or Version 2 of the DANSR assay uses
9 Dr. Stuelpnagel and Oliphant's invention of allele-specific
10 extension and ligation. Correct?

11 A. If we emphasize that extension part, then yes.

12 Q. And that's the part that they emphasized; wasn't it?

13 A. Well, I don't know. They talked really about the overall
14 process, about extension and ligation; but yes.

15 Q. And even though you claim that they were inventors on
16 Claim 1, you never made the claim -- and you don't now -- that
17 Ariosa actually uses that process. Correct?

18 A. I believe they use Claim 1, but they clearly don't use
19 extension.

20 Q. Okay. Let's explore that a little bit. And I want to do
21 it this way. What I heard at the beginning of your testimony
22 was that Dr. Stuelpnagel and Oliphant are inventors of
23 Golden Gate. Then you say Golden Gate is covered by the claims
24 of the '794 patent; therefore, they must be inventors of the
25 '794 patent. Right?

1 A. I believe that was one part of the evidence, yes.

2 Q. So it's kind of like a little transit of property of
3 inventorship?

4 A. Again, that was one part of the evidence that we talked
5 about.

6 Q. Now let's -- I want to give you a hypothetical. And
7 that's fair for experts -- right? -- to ask a hypothetical
8 question?

9 A. I don't know what the rules in court are.

10 Q. Okay. Well, let me ask you this question. Let's say that
11 we have a claim that says, *Provide target sequences, and then*
12 *hybridize those target sequences with probes.* Okay? Can you
13 imagine that claim?

14 A. Okay.

15 Q. You'd agree that that claim would cover Golden Gate;
16 wouldn't it?

17 A. I mean, I -- not without sitting down and doing a thorough
18 exam. I mean, just those two statements, I don't think, would
19 constitute --

20 Q. Well, sir, this would be a much more broad claim than
21 Claim 1. Right? Because Claim 1 has probes. Claim 1 has
22 target sequences. Claim 1 has hybridizing the two. And it has
23 a lot more to it. Right?

24 A. Sure. I guess I'm not understanding where you're going
25 with that.

1 Q. Well, just a simple question. If the claim just said,
2 *Provide targets. Hybridize them with probes* -- that's
3 something that Golden Gate does. Correct?

4 A. It hybridizes probes and targets. Yes.

5 Q. Correct. So that claim would cover Golden Gate. Correct?

6 A. I suppose if this were considered to be a legitimate
7 claim. It's hard to imagine the Patent Office would surmise
8 something like that, but --

9 Q. But under your reasoning, because Dr. Stuelpnagel and
10 Oliphant were inventors of the Golden Gate product, and because
11 that product would be covered by this claim, somehow, that
12 would mean that Drs. Oliphant and Stuelpnagel invented
13 hybridizing target sequences with probes. Correct? That's
14 your reasoning?

15 A. I'm not following this. Say that again.

16 Q. So because Dr. Stuelpnagel and Oliphant were inventors of
17 Golden Gate, under your reasoning, they would be inventors of a
18 claim that simply requires hybridizing target sequences with
19 probes. That's your reasoning. Correct?

20 A. No, because, I mean, there are other factors that are
21 important. For example, were they named inventors on the
22 patent? Did they sign an oath of inventorship on that
23 application? And all of these factors, I think, are relevant.

24 Q. So we can't assume and say, *Well, they invented Golden*
25 *Gate.* Golden Gate, under your view, is covered by the claim;

1 therefore, they must be inventors. That would be a logical
2 fallacy. Right?

3 **A.** Well, again, out of context, it's hard to say; but in this
4 context, I think it's fair.

5 **MR. HEINRICH:** I'm going to go on to a new topic.
6 Maybe we can take our --

7 **THE COURT:** All right. Ladies and gentlemen, we'll
8 take our afternoon recess at this time. So we won't see you
9 again until Monday, but we should see you on Monday, regardless
10 of politics. And we are on track to finish when we told you,
11 but that's why everybody's getting so anxious now. So we'll be
12 back at 8:30.

13 In the meantime it's really important that you not discuss
14 this with each other, with anyone else. Don't do any research.
15 Don't let people talk to you. We're very close to the end, but
16 we're not there yet. So have a great weekend. We'll see you
17 8:30 Monday morning.

18 (Proceedings were heard outside the presence of the jury:)

19 **THE COURT:** We need you 8:30 in the morning, too,
20 sir.

21 (Witness excused, subject to recall.)

22 **THE COURT:** All right. We'll be in recess.

23 (At 3:28 p.m. the proceedings were adjourned.)
24
25

1 I certify that the foregoing is a correct transcript from the
2 record of proceedings in the above-entitled matter.

3
4 

5 January 18, 2018

6 Signature of Court Reporter/Transcriber Date

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